THE American JOURNAL OF Surgery

JANUARY 1955

THURSTON SCOTT WELTON, M.D., EDITOR

Symposium on Bronchopulmonary Diseases

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SIXTY-FOURTH YEAR OF PUBLICATION

JANUARY 1955

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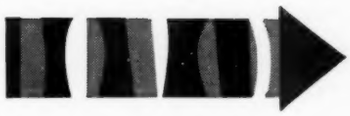

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The American Journal of Surgery is published monthly by The American Journal of Surgery, Inc., 49 West 45th Street, New York 36, N. Y. Yearly Subscription, $15.00 U. S. A.; $16.00 Canada; $17.00 Foreign including Pan-American Countries. Single Numbers $2.00; Special Numbers $4.00. Reentered as second class matter February 7, 1951, at the Post Office, New York, N. Y., and on February 7, 1951, at York, Pa., under the Act of March 3, 1879. January, 1955—New Series, Volume 89, No. 1. *Copyright, 1955, by The American Journal of Surgery, Inc.*

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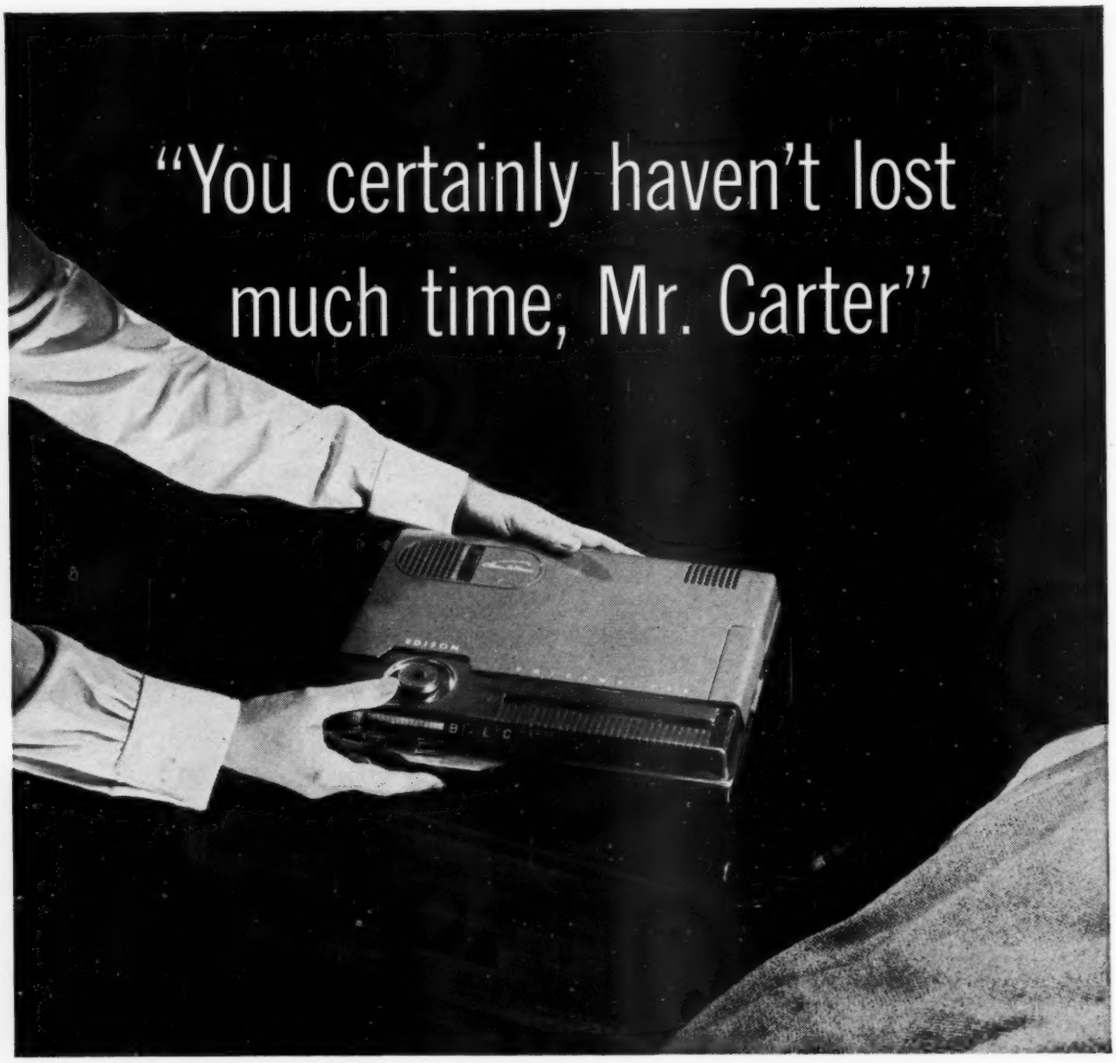

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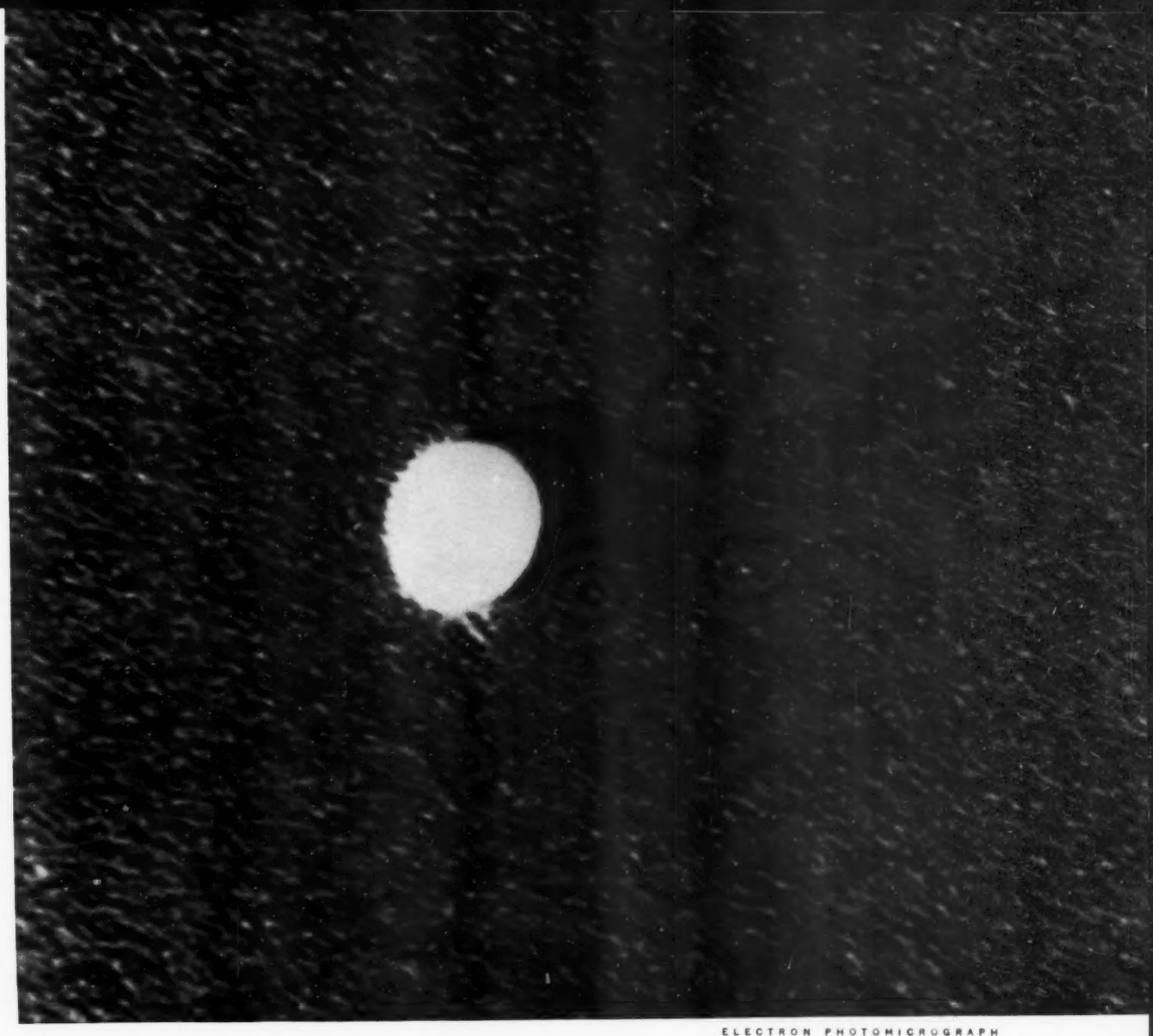

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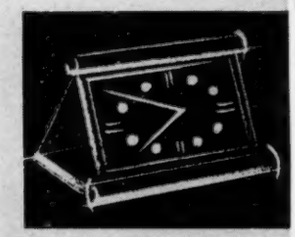

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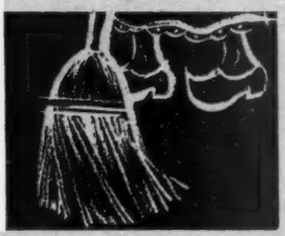

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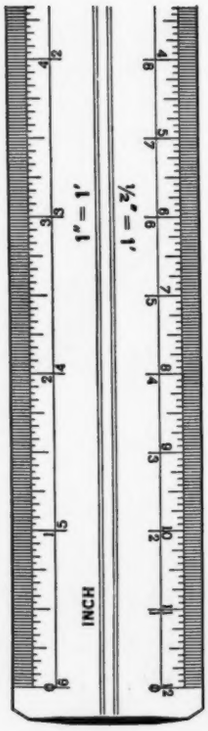

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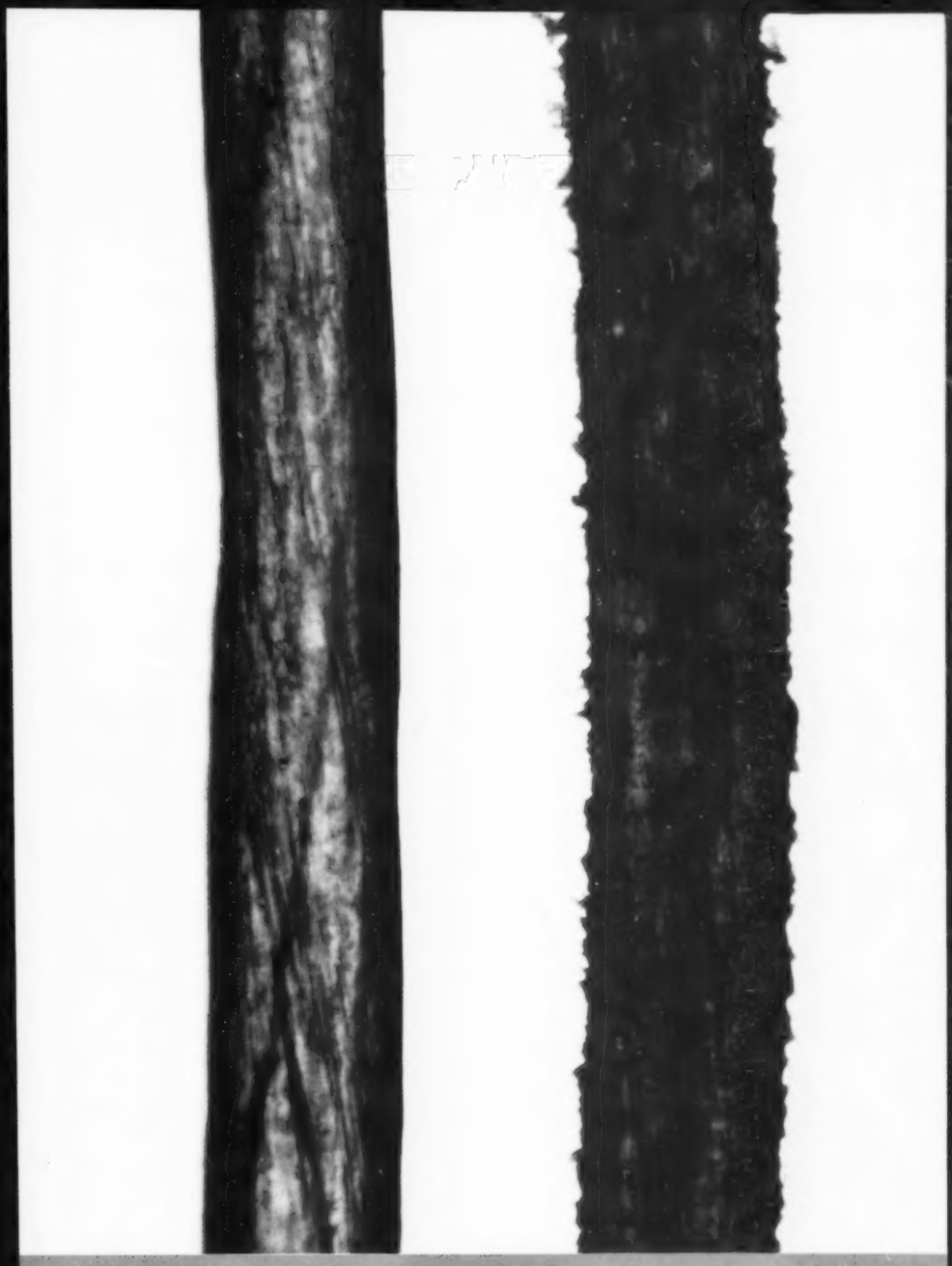

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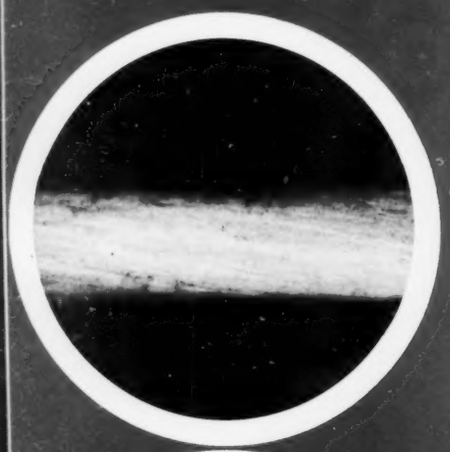
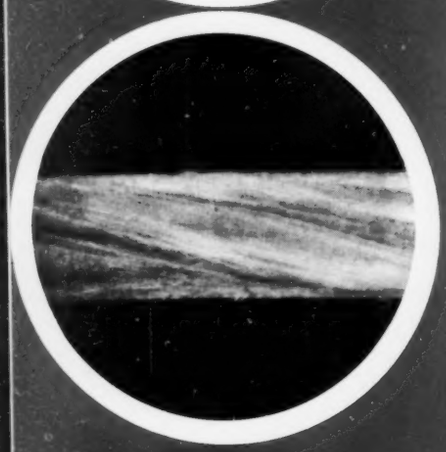


D & G GUT

Firm, even cohesion of plies is apparent in this photomicrograph of a D & G SURGICAL GUT suture.
Reason: plies were twisted into a strand before suture was chromicized. Natural cohesive forces of moist untreated collagen firmly bond the plies together and hold the twist.
Result: under stress, plies of the suture hold together. The D & G gut is more flexible and knot strength is greater.



ANOTHER LEADING GUT

Photomicrograph detects separate and distinct plies in a strand of another leading brand of surgical gut. Here each ply was chromicized before they were twisted into suture strands. Such "ribbon chromicizing" hardens the surface of each ply, decreasing the natural bonding action, lowering the flexibility and tensile strength of the suture.

Photomicrographs (unretouched) by E. J. Thomas, Stamford Laboratory of the Research Division of the American Cyanamid Company, Stamford, Conn.

Method used: dark field, reflected illumination, focus on crest of surface, 38 x. Material used: medium chromic gut, size 00.

see exhibit on previous page

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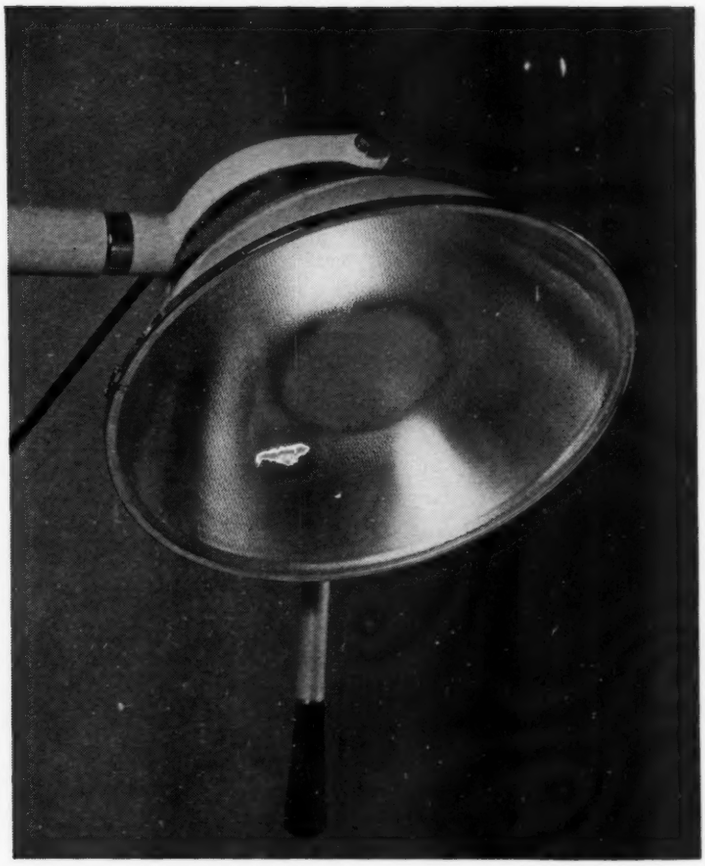

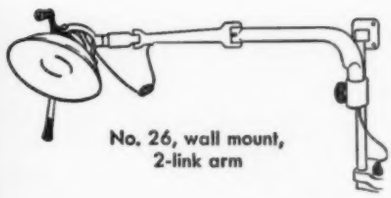

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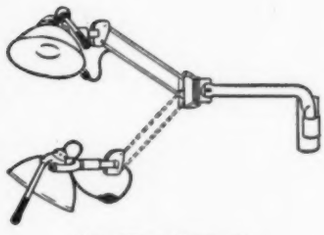

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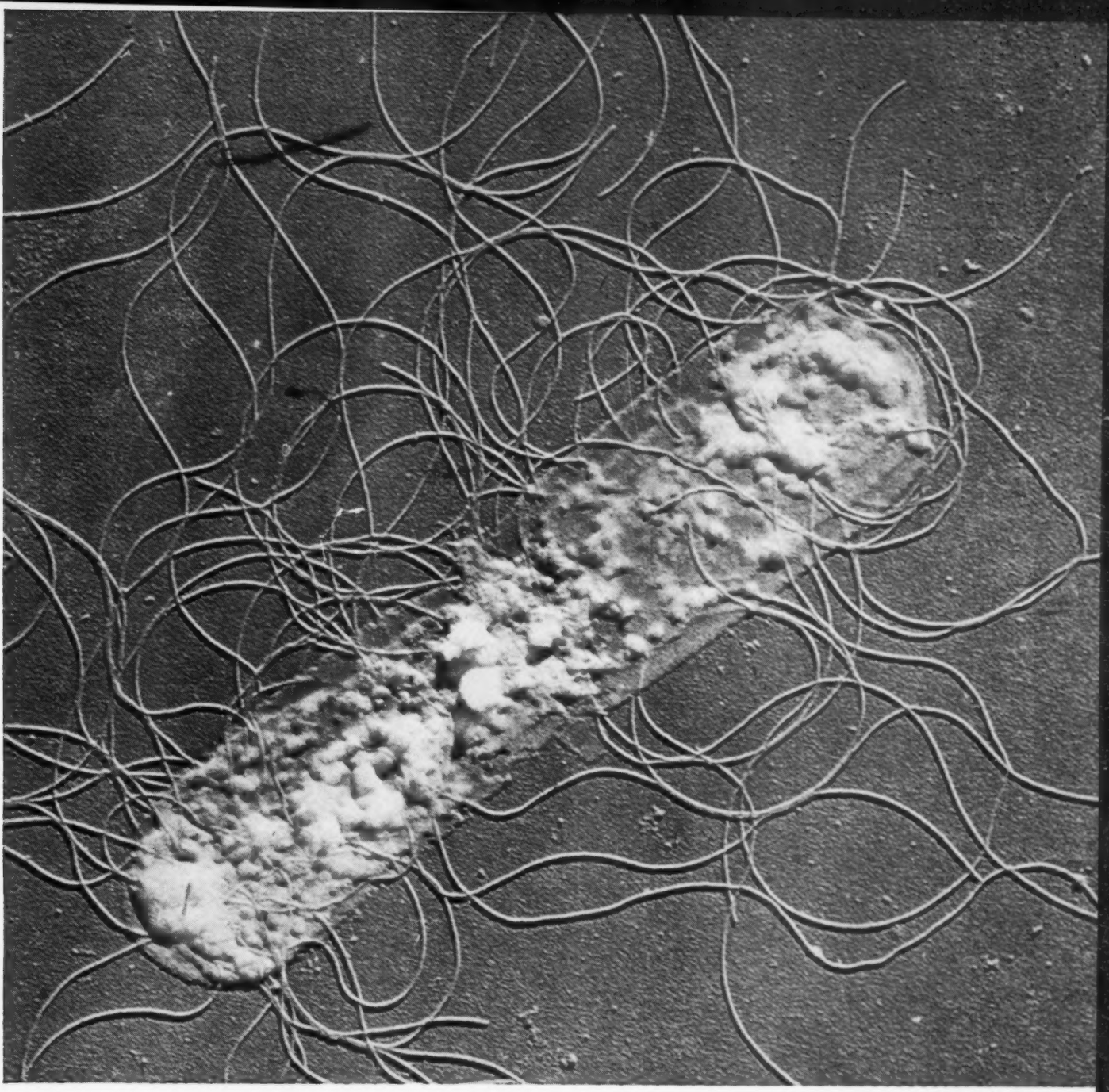

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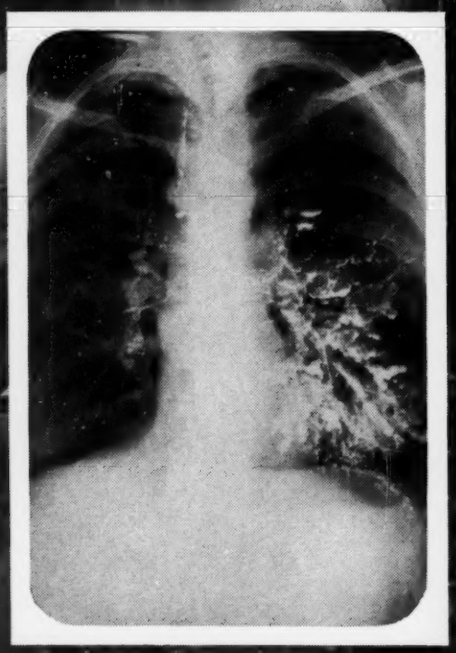

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Singer, J. J.: Differential Diagnosis of Chest Diseases, Philadelphia, Lea & Febiger, 1949, pp. 1953-4.

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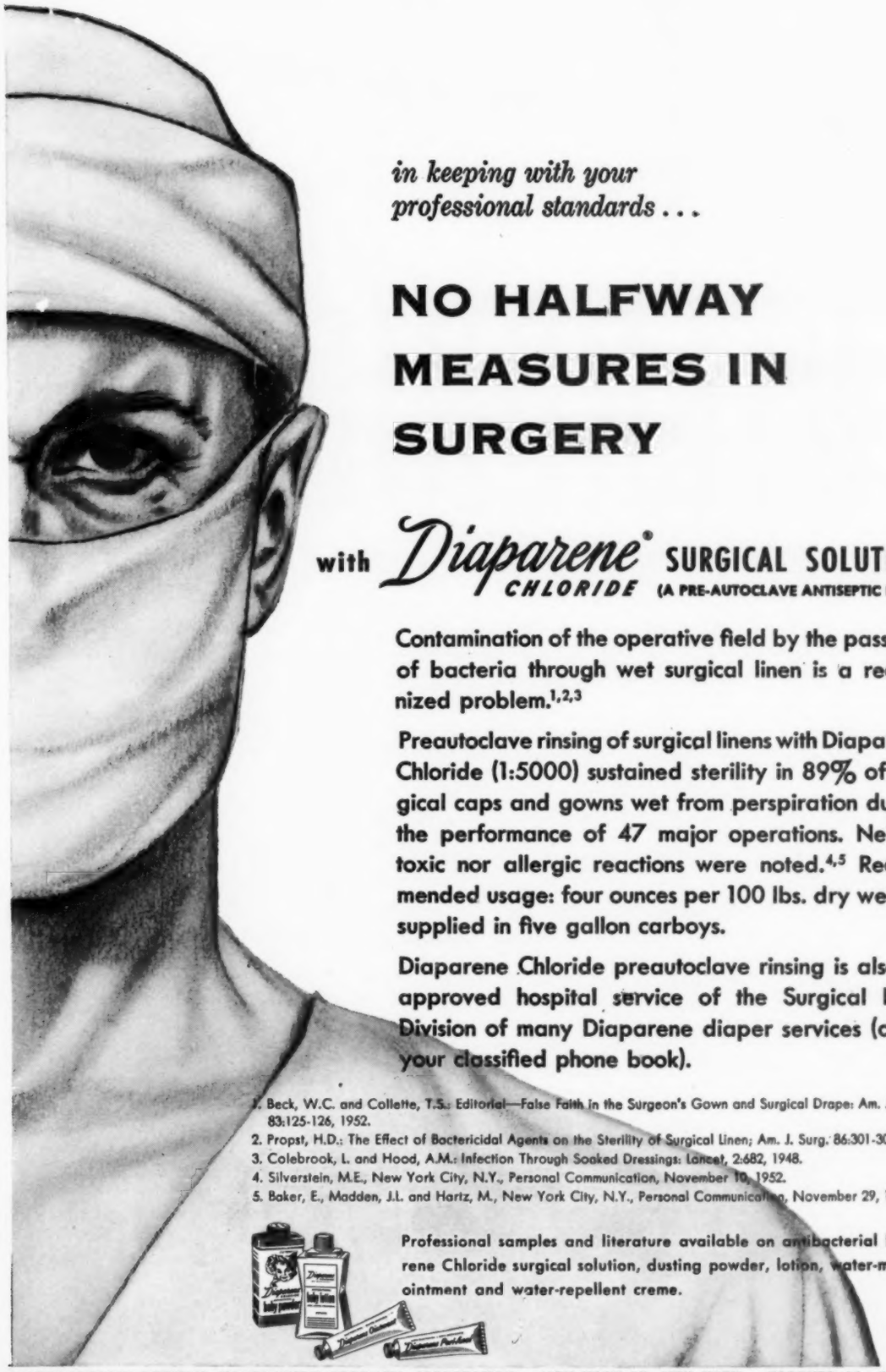

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1. Beck, W.C. and Collette, T.S.: Editorial—False Faith in the Surgeon's Gown and Surgical Drape: Am. J. Surg., 83:125-126, 1952.
2. Propst, H.D.: The Effect of Bactericidal Agents on the Sterility of Surgical Linen; Am. J. Surg. 86:301-308, 1953
3. Colebrook, L. and Hood, A.M.: Infection Through Soaked Dressings: Lancet, 2:682, 1948.
4. Silverstein, M.E., New York City, N.Y., Personal Communication, November 10, 1952.
5. Baker, E., Madden, J.L. and Hartz, M., New York City, N.Y., Personal Communication, November 29, 1954.

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1. Dearing, W. H., and Needham, G. M.: Proc. Staff Meet., Mayo Clin. 28:507 (Sept. 9) 1953.
2. Bargen, J. A.: Surg., Gynec. & Obst.: 99:373 (Sept.) 1954.

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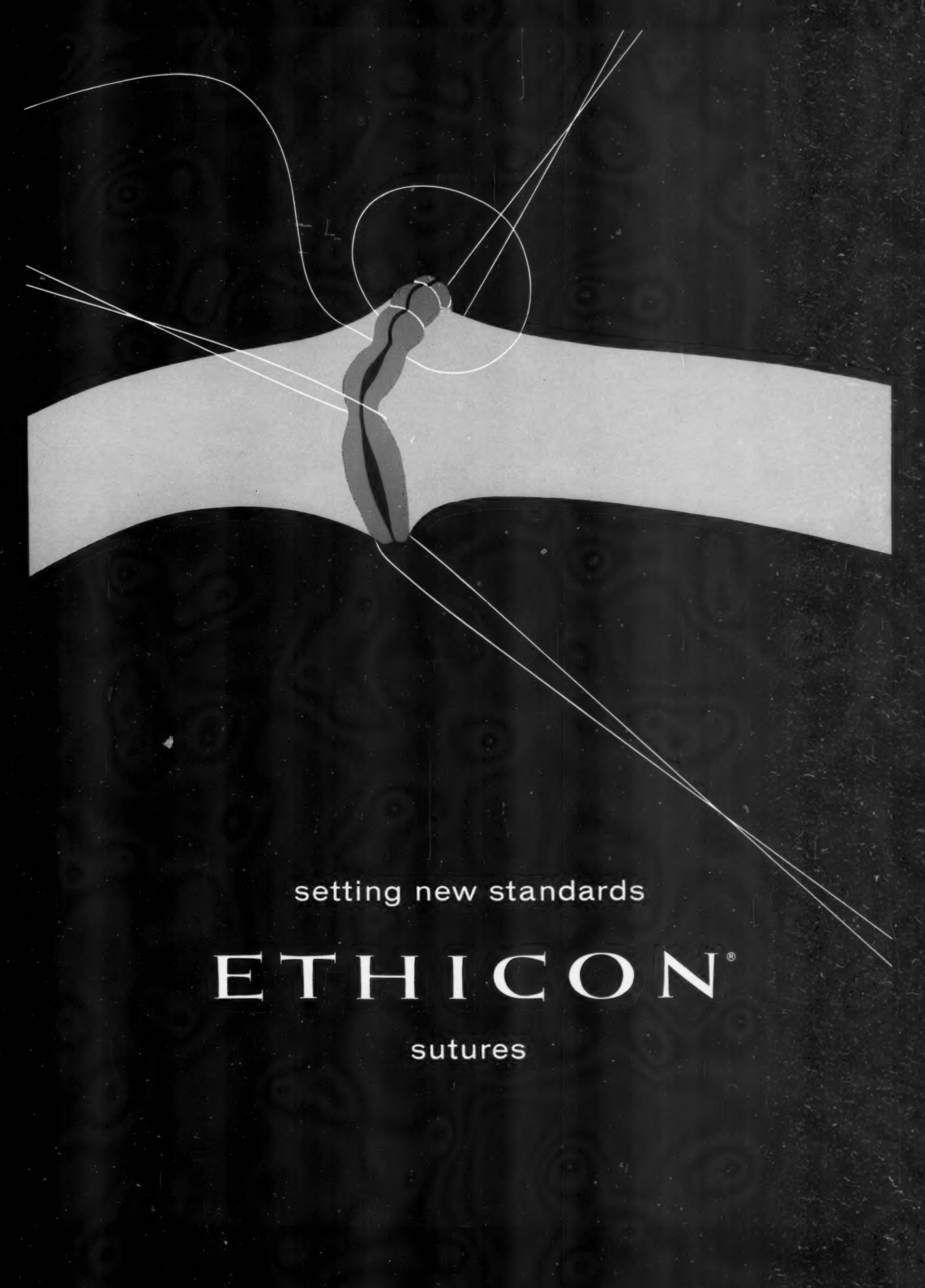
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*Sherber, D. A.: The Control of Bleeding, Am. J. Surg. *86*:331 (Sept.) 1953.

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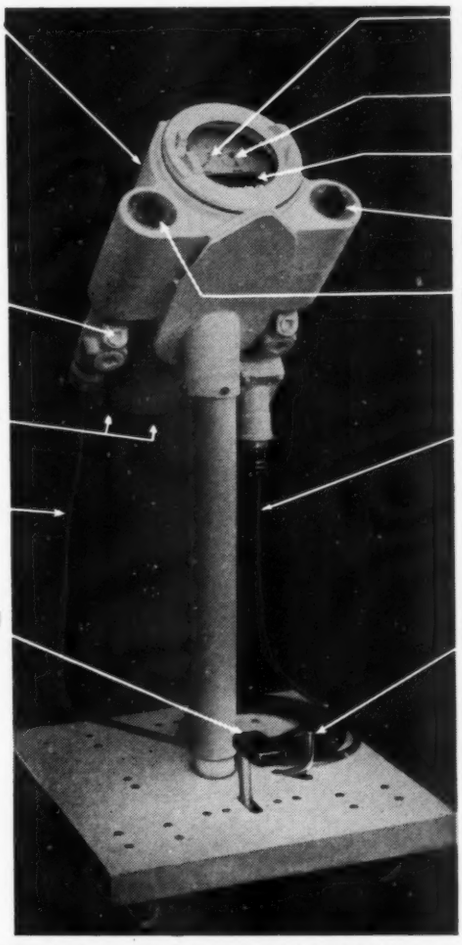

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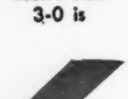

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It is another of the more than 30 organisms susceptible to

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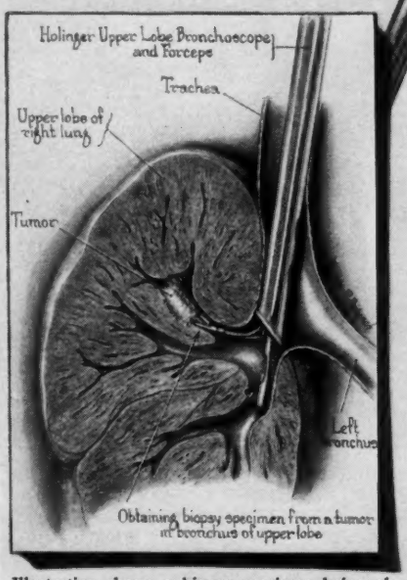

Holinger Upper Lobe Bronchoscope and Forceps
Trachea
Upper lobe of right lung
Tumor
Left bronchus
Obtaining biopsy specimen from a tumor in bronchus of upper lobe

Illustration shows a biopsy specimen being obtained from a tumor with the Holinger upper lobe biopsy forceps.

WRITE FOR LITERATURE DESCRIPTIVE OF THE MANY OTHER TYPE FORCEPS.

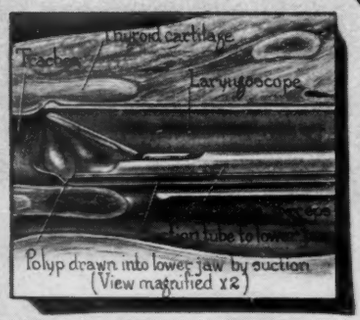
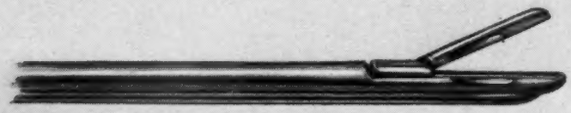
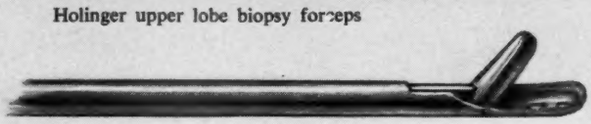


Illustration shows a polyp drawn by suction into lower jaw of Broyles laryngeal suction forceps.

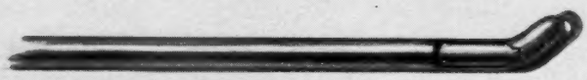


Broyles laryngeal suction forceps

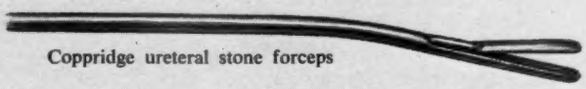
Holinger upper lobe biopsy forceps



Lowsley grasping forceps



Turell rotating rectal biopsy forceps



Coppridge ureteral stone forceps

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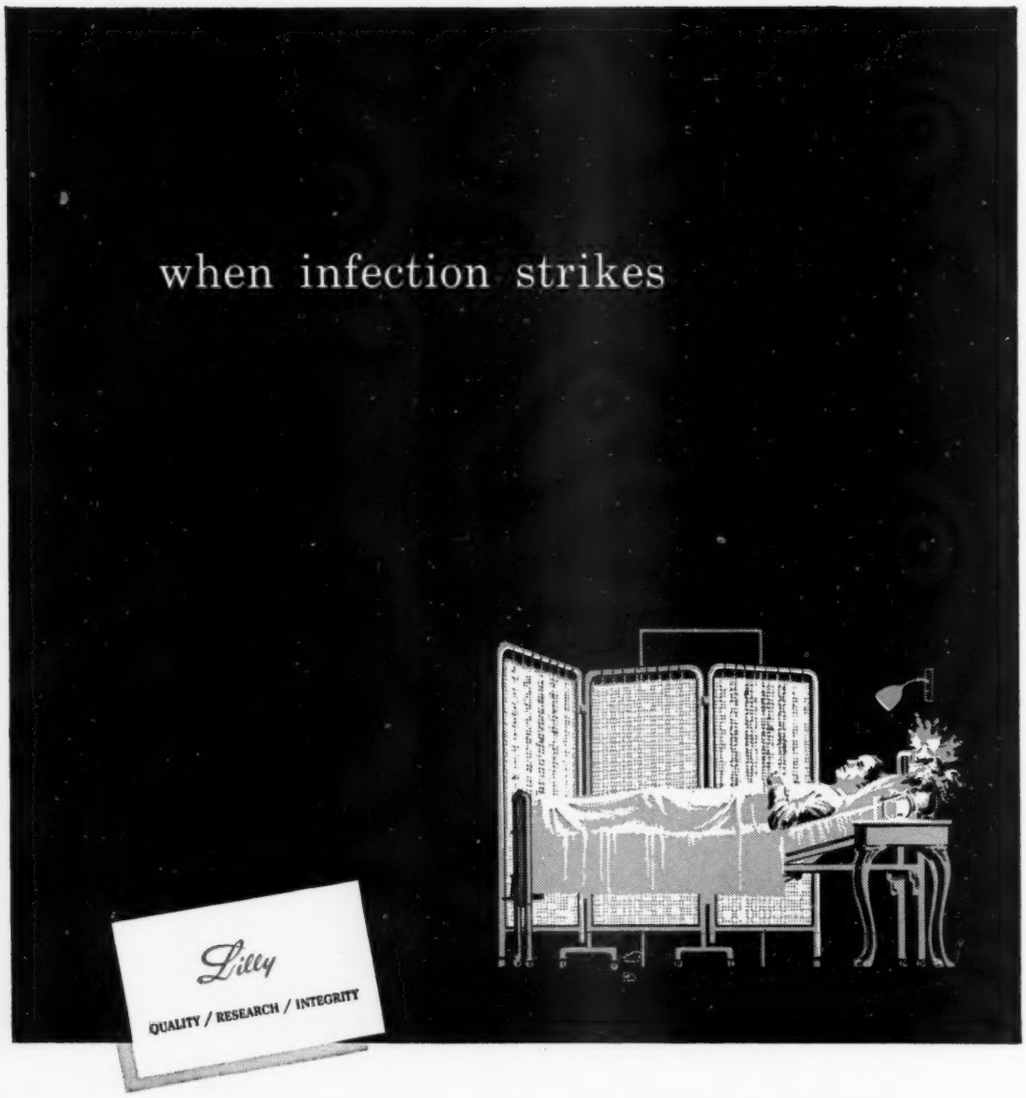

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VOL. 89 JANUARY 1955 NUMBER ONE

FUNDAMENTAL CONSIDERATIONS IN PULMONARY SURGERY

Surgery in Our Increasing Knowledge of Pulmonary Disease

WILLIAM A. HUDSON, M.D., *Detroit, Michigan*

THE universal attempt by humanity to obtain relief either through self-medication or through the help of others in time of sickness or injury is based upon a deep-lying instinct in human nature that leads to the conviction that relief from suffering is an obtainable goal. The great majority of people of ancient times looked upon disease as a calamity brought about by supernatural forces. Mysterious powers beyond human understanding being considered the underlying cause of disease, the treatment of disease was naturally in the hands of persons well versed in supernatural matters. Thus the history of medicine is rich in examples of human fallibility and error. The history of the advancement of medical science, however, is the history of the discovery of a number of important fundamental principles leading to new views of disease, to the invention of new instruments, devices and procedures with adaptations to conform with the needs of changing times and conditions and the mental attitudes of the time. This has been accomplished by the arduous labor of devoted workers blessed with alert, inquisitive minds and spurred on by a desire to learn. The development of medical science has been neither continuous nor progressive but rather like a tangled and tortuous trail with many obstructions. Ideas of the greatest scientific moment have been choked at birth or veered into a blind alley through some current prepossession or deprived of their chance of fruition through human indifference, narrowmindedness or other accidental circumstances.

It is no exaggeration to say that advance in medical science is in large part due to shining individualism. The whole art of medicine lies in observation. Hippocrates demonstrated the value of complete study, observation and accurate records; this is illustrated by his description of the physical findings and symptoms of cough, purulent sputum, dyspnea, intermittent fever, profuse sweat and anorexia with the succussion sign as he observed them in his patients afflicted with symptoms refer-

able to the chest. The accuracy of his observations and descriptions is such as to enable one at this late date to make a differential diagnosis between empyemas thoracis and pyopneumothorax. The value of careful observation and accurate records is seen in the records left by numerous other authors of ancient times. The way of thinking of the Old Art of healing came so near to the truth that one should take it more into consideration and wonder at the diagnoses made.

It is true that occasionally snap judgment based upon a chance or passing observation may lead to a correct diagnosis, but it is well to remember that the overlapping of symptoms and physical findings in many diseases makes it desirable that no source of information should be overlooked. Hippocrates, Ambroise Paré, John Hunter and Lord Lister served humanity through the exercise of a keen, watchful eye, tactful fingers and an alert ear, supported by a logical mind.

"There is nothing men will not do." There is nothing they have not done to recover their health and save their lives.

As the ancient Greeks hung upon the teachings of Empedocles and Hippocrates, and as humanity responded to the ideas of Jenner, Pasteur and Lister, so there has been at no time a greater interest in the advancement of medicine than in our time. However, under the best conditions it is still possible and probable that many highly intelligent and highly educated persons will continue to hug their whims and superstitions, consult quacks and be otherwise amenable to absent treatment and action at a distance. "To folk-medicine, doubt is unknown—it brings the peace of security." The ability of the physician to hold the confidence and complete trust of peoples of all classes and races is dependent upon his ability sincerely to project his thinking and expressions to the level of the patient that the patient may have a clear idea as to the problem (disease) that is to be met. The soundness of the physician's judgment depends upon his knowledge of the experiences of men of past ages as well as upon his own previous experiences and his ability or capacity to learn or profit from experience.

Primitive pathology ascribed disease to something projected into the body of the victim, something taken from it, or to the effect of sorcery upon some part of or some object connected with the body of the patient. Primitive man's wounds were dressed with moss or fresh leaves, ashes or natural balsams, and when poisoned he was treated by sucking or cauterization. Cupping was performed by means of animal horns. In seeking an artificial paradise by means of narcotics and intoxicants like alcohol, opium, hashish or mescal, priority certainly belongs to primitive man. Medicine is curiously indebted to the non-medical man for many of its innovations. It learned from a Monk how to use antimony; from a Jesuit how to cure agues; from a Friar how to cut for a stone; from a dairy-maid how to prevent smallpox. Primitive man was dependent upon the method of trial and error in his early search for relief from suffering, but the human race is fortunately endowed with the power to convey the results of experiences through speech and records from one generation to another. The result has been an ever increasing and widening fund of knowledge and a clearer understanding of the cause and the cure of the diseases and afflictions of the human race.

Progress in our ability to diagnose and cure diseases of the chest was very slow until the early part of this century. The introduction of aseptic surgery and controlled anaesthesia combined with an increasing knowledge of the anatomy and function of the thoracic organs opened the way for a few bold individuals to invade the thorax surgically with the result that we have been able to study the changing physiologic and pathologic conditions in the living patient and under all sorts of environments.

X-ray studies with and without contrast media, combined with the multitude of bacteriologic and functional studies which have been developed to aid in the differential diagnosis of thoracic disturbances, have assumed an increasing importance in a search for information concerning diseases of the chest. The correlation of the findings at the time of surgery with the preoperative diagnosis or impression has led to a keener appreciation of the significance of the preoperative clinical and physical findings in diseases of the chest.

The following series of cases is presented to emphasize these facts:

CASE REPORTS

CASE 1. W. H., an eighteen year old white boy, complained of inability to run at top speed for 100 yards. Routine x-ray of the chest

led to a diagnosis of a collapsed right lung. He was short of breath. The right hemithorax was definitely fuller in all dimensions than the left. The respiratory movements on the left were free; on the right they were restricted. The percussion note was impaired throughout the left and was hyperresonant from the right well to the left of the midline. Fluoroscopic and x-ray studies revealed an area of decreased density occupying the right hemithorax with the mediastinum and the heart displaced far to the left. A few indistinct linear markings were observed throughout this area of decreased density, and at the right apicomediastinal junction there were unmistakable pulmonary markings. The right hemidiaphragm was very flat and immobile. Bronchoscopic studies revealed a displacement of the left stem bronchus to the left, and the orifices of the right middle and lower lobe bronchi were slit-like openings. There was very little inflammation. At operation a large pulmonary cyst with the right lower lobe was removed. The middle and upper lobes were free of disease. The mediastinum and its contents returned to the midline.

The original interpretation of the x-ray studies failed to take into account the presence of definite but indistinct pulmonary markings throughout the area of decreased density. The result was a missed diagnosis of collapsed lung, pneumothorax, when in reality the involved portion of the lung was overinflated.

Failure to note such markings has led numerous men to needle cysts of this character with disastrous complications.

Case II. H. M., a forty-eight year old white man, was admitted with the chief complaint of shortness of breath. The patient was obviously short of breath and his lips and nails were severely cyanotic. There was no clubbing of the fingers. The right hemithorax was fuller than the left. There were distant vesicular breath sounds throughout the right hemithorax with numerous musical notes. The heart sounds were clear with no murmurs. X-ray and fluoroscopic studies revealed numerous areas of decreased density throughout the right hemithorax with some rather prominent linear markings traversing these areas. The right hemidiaphragm was flattened. Bronchoscopic studies revealed a slit-like opening of the right upper lobe bronchus with very little inflammation. At operation multiple large cysts of all lobes of the right lung were found. Right pneumonectomy was performed. The patient has shown much improvement in his work tolerance.

These areas of decreased density frequently reveal horizontal lines simulating a fluid level and have occasionally been drained. Many times they become secondarily infected. Several thoracotomies may be performed before someone hits upon the correct diagnosis.

Case III. A. G. N., a sixty year old white man, complained of shortness of breath increasing over a period of two years to the extent that he had given up work. The patient was obviously very short of breath with some cyanosis of his lips and nail beds. His right hemithorax was fuller than the left and was fixed. The heart was displaced to the left. X-ray and fluoroscopic studies revealed an area of increased markings extending from the right hilum to the periphery along the first rib anteriorly; distal to this was an area of decreased density with a few pulmonary markings traversing the right lung field. The right hemidiaphragm was flat and fixed. The mediastinum was shifted to the left. The vital capacity was 56 per cent. Bronchoscopic studies revealed a mild inflammatory reaction on the right. At operation the right upper lobe of the lung was removed because of a large cyst occupying the entire upper lobe. The patient has since returned to his work. Microscopic studies revealed low grade inflammatory reaction of the walls of the cyst.

Earlier recognition of this condition would have saved this individual from a forced retirement. He has now returned to his business.

Cystic disease of the lung with bivalve obstruction may produce symptoms simulating the symptoms produced by other diseases, but careful study of details will lead to a correct diagnosis.

Case IV. B. M., a sixty-seven year old white woman, complained of soreness of the chest and pain in the heart with gas on the stomach for a period of about six months. She gave a history of having been treated for tuberculosis at the age of twenty-eight years. The patient had the general appearance of being well but was somewhat nervous (she was undergoing psychiatric treatment). There were a few scattered rales at the right base posteriorly near the midline. Fluoroscopic and x-ray studies revealed an area of increased

density confluent with the right heart border. There was no shifting of the density during respiratory movements. Bronchoscopic studies revealed some displacement of the medial bronchial division lateralward but there was no obstruction. Lipiodol studies confirmed the bronchoscopic findings. The impression formed was that we were dealing with a benign mass; that the symptoms were probably exaggerated; and that surgical intervention was not indicated, even though the psychiatrist believed otherwise. Trauma without marked relief offered too great a chance for the patient to become more disturbed.

Case v. H. D., a sixty-four year old white woman, complained of pain in the chest which was worse after eating (she had had her gallbladder removed four years before). The patient regurgitated food at times, usually food that she had just eaten. Her chest seemed to swell just under the heart at times. She was very heavy (214 pounds) and was short of breath. The pulse was rapid but of good volume. The lung fields were resonant and there were scattered musical notes throughout both fields. On percussion the outline of the heart was within the limits of normalcy. X-ray and fluoroscopic studies revealed an area of increased density continuous with the diaphragmatic shadow near the midline and overlying the heart shadow to the left of the midline. It was roughly ovoid in shape. Lateral films revealed a wide postcardiac space with some increase in density. Esophagoscopy revealed the esophagus to be normal with very little inflammation. Barium studies revealed the barium to enter the stomach directly from the esophagus, but in the Trendelenburg position a portion of the stomach was found to lie in the mediastinum to the left of the esophagus. At operation it was found that there was a hiatal ring and that the stomach entered the mediastinum anteriorly and to the left of the esophagus through a break in the diaphragmatic muscle fibers leaving the hiatal ring intact. The peritoneum advanced into the mediastinum ahead of the stomach and omentum. The defect was repaired.

Patient B. M. (Case iv) was not operated upon because of her age and the mental problem present and the rather mild symptoms of which she complained, whereas patient H. D. (Case v) had definite symptoms and stood to be benefited by repairing the defect. The whole patient must be considered in any proposed plan of treatment.

Case vi. H. V., a fifty-seven year old white man, was admitted with the chief complaint of unresolved pneumonia. Diagnosis of pneumonia was first made four months previously. The patient had run a fever up to 101°F., with loss of weight and general weakness. There was soreness in the area of the right shoulder blade. The patient was somewhat underweight and was outwardly short of breath but there was no cyanosis. His voice had a brassy quality. The right upper thorax was somewhat limited in expansion and the percussion note was flat. The breath sounds were absent above the second rib and above the spine of the scapula posteriorly on the right. Elsewhere the percussion note was resonant. No rales were heard. The heart sounds were clear and no murmurs were heard. X-ray and fluoroscopic studies revealed a roundish mass filling the right chest above the upper border of the third rib. Bronchoscopy revealed fixation and marked narrowing of the orifice of the right upper lobe bronchus. At operation the upper lobe was solid with firm adhesions between the chest wall and the mediastinum with a tumor invading the pleura along the superior vena cava. The lung was removed with the involved pleura and lymph nodes. Microscopic diagnosis was small round cell carcinoma.

A diagnosis of unresolved pneumonia is seldom expressive of the real disease present. A pneumonia that fails to respond as one might expect should be re-evaluated. Bronchoscopy will frequently give a clue to the underlying condition which is frequently an obstructive lesion.

Case vii. F. P., a fifty-six year old white man, complained of cough with sputum, fever, poor appetite, loss of weight and hiccoughing. The patient was weak and had a constant hacking cough productive of yellow pus. There was a flattening of the left upper chest anteriorly with limited motion. The percussion note was flat over the entire left hemithorax and the breath sounds were but faintly heard near the apex. The heart sounds were clear but the rate was 100. The sputum was negative for tubercle bacilli. X-ray and fluoroscopic studies revealed an area of increased density occupying the lower half of the left lung field. The heart and mediastinum were displaced to the right, and the left hemidiaphragm was

elevated and fixed. Bronchoscopic studies revealed funnel-like narrowing and fixation of the left stem bronchus. At operation a mass was found to occupy the left hilar area and the entire lower lobe of the lung with encroachment upon the upper lobe bronchus. The lower lobe bronchus was obstructed. A tumor had grown from the hilar area along the bronchial wall toward the periphery of the lung. The parenchyma contained numerous abscesses. The phrenic nerve was caught up in the inflammatory adhesions. Microscopic diagnosis was squamous cell carcinoma, grade 2.

The displacement of the heart and mediastinum to the right led to an earlier diagnosis of empyema. The massive drowning of the lung actually led to an increase in pulmonary volume with displacement of the heart in the opposite direction even in the face of bronchial obstruction. The obstruction of the bronchus was ample indication for thoracotomy for removal of the obstructed portion of the lung. The removal of the lung resulted in immediate loss of fever.

Symptoms and physical findings that do not conform to the expected pattern are of significance and should never be explained away.

Case viii. D. G., a fifty-two year old white man, was first seen four years ago complaining of a hard cough over a period of three weeks. Physical findings were essentially negative. X-ray and fluoroscopic studies revealed some prominence of the right hilar area. The left lung was clear. Bronchoscopy revealed a mild inflammatory reaction of the right bronchi. It was decided that the lesion was inflammatory and the patient was treated with antibiotics, with relief and reduction of the shadow in the right hilar area. Four years later, after periodic observation with no physical or roentgenologic changes, the patient complained of a burning in his left upper chest. Physical findings revealed a few scattered rales at the left apex. X-ray and fluoroscopic studies revealed an area of increased density at the left apex and bronchoscopy revealed no fixation or distortion of the bronchial tree. The sputum was negative for tubercle bacilli. At operation a bilobular mass was found in the posterior segment of the upper lobe and some enlarged hilar lymph glands were removed. Left upper lobectomy with removal of the lymph glands was performed. Microscopic diagnosis was adenocarcinoma, grade 3.

Six months later the patient died of proved carcinomatous metastasis to the left temporal area.

Carcinoma may simulate any one of a number of diseases and one should always be conscious of this tumor.

Case ix. N. S., a sixty-seven year old white man, complained of cough with necessity of clearing his throat all the time. The patient appeared well, and except for an occasional rale in his mid-lung field on the right the findings were essentially negative. X-ray and fluoroscopic studies revealed some prominence of the right hilar area. There were no tubercle bacilli in the sputum. Bronchoscopy revealed some edema of the orifice of the right middle lobe bronchus with some pus and mucous present. At operation the right middle lobe was removed, cutting through what appeared to be healthy bronchus. The microscopic study revealed squamous cell carcinoma, grade 3. Seven years later, because of shortness of breath, a large gland was removed at the bifurcation of the trachea. This proved to contain squamous cell carcinoma. The patient continues to do well.

This patient was originally operated upon because of a persistence of his productive cough. The response to the second operation is ample evidence of the importance of always doing that which offers a chance to make the patient comfortable.

Case x. I. L., a sixty year old white female, was told by a tuberculosis specialist that she had a spot on her right lung. The patient was well nourished. There was no apparent discomfort. The percussion note was dull at the right apex with breath sounds distant. The left lung was clear. There were no heart murmurs. X-ray and fluoroscopic studies revealed an area of increased density above the third rib anteriorly on the right. The diaphragmatic movements were free and equal and synchronous. Bronchoscopic studies revealed a reduction in the size of the right upper lobe bronchus with fixation of the wall. At operation the right upper lobe was removed. An obstruction was found in the posterior and apical bronchial divisions. Microscopic study revealed it to be an infiltrating undifferentiated cell carcinoma; also, chronic pneumonitis with abscess formation.

Two years later cough developed with sputum which was reported negative for

tubercle bacilli. There was a high fever (105°F). Bronchoscopic study revealed an obstruction to the right lower lobe bronchus. Microscopic sections revealed no carcinoma but the secretions collected at bronchoscopy revealed tubercle bacilli. Treatment with antibiotics relieved the obstruction and converted the sputum. The patient is again well.

This case illustrates two points: (1) a failure to recognize evidence of bronchial obstruction due to carcinoma; (2) in the second illness the table was turned and it was through direct study by bronchoscopy that the diagnosis of tuberculosis was established and recurrent carcinoma ruled out for the time being.

Symptoms of bronchial obstruction can be produced by any lesion which causes a blocked bronchus. It is necessary for the physician to make himself acquainted with such symptoms. Once a diagnosis of bronchial obstruction is made the cause can be determined.

CASE XI. B. C., a fifty year old Negro woman, was told twelve years before that she had something wrong with her left lung. There was gradual loss of endurance with shortness of breath but very little pain. Her heartbeats were fast. The patient was slow and deliberate in all her movements. She talked very little and then with obvious respiratory distress. There was a non-productive cough. The left hemithorax was much fuller than the right and there was limited expansion on the right. The left had little if any expansion. The percussion note was flat throughout the left, anteriorly and posteriorly. Fremitus was absent on the left, as were breath sounds. On the right the breath sounds were vesicular and distant; the percussion note was impaired and fremitus increased. X-ray and fluoroscopic studies revealed an area of uniformly increased density occupying the entire left hemithorax and extending well into the right hemithorax. At the left apex there was a narrow border suggestive of air containing lung. The vital capacity was 47 per cent. Bronchoscopic studies revealed the right stem bronchus to be displaced to the right with narrowing of the lumen. The left stem bronchus had but a slit-like opening. No masses were observed. At operation a large cyst containing hair, sebaceous material and other structures was removed. It arose from the mediastinum and derived its blood supply from a small artery that seemed to arise from the aorta. The left lung was not primarily involved and was preserved. The patient is well. This patient had been told that nothing could be done to relieve her of her tumor.

Patients have the right and privilege of deciding whether they wish to try to rid themselves of their disease. When surgical intervention offers hope of relief, the surgeon should not permit statistics to interfere with the proper attempt to help the patient. The will to live is present in all people.

CASE XII. C. G. was a fifty-one year old white woman. X-ray at a routine health check-up revealed a shadow in the left chest. The patient said that she had hoarseness when she was tired. The patient had the appearance of good health. The physical findings were essentially negative. X-ray and fluoroscopic findings revealed a globular-shaped density overlying the shadow of the arch of the aorta on the left. Bronchoscopy revealed no deformity of the vocal cords or of the tracheobronchial tree. At operation there was a globular mass lying on the left near the transverse process of the seventh thoracic spine. It obscured the foramen but it did not extend into it. The mass was connected with the sympathetic trunk by several fine nerve fibers. On section the tumor was of a deep orange color and was well encapsulated. Microscopic sections revealed the tumor to be a neurofibroma.

A benign mass in the chest can be as deadly as a malignant process if it is permitted to grow to such a size that it interferes with the function of vital organs.

CASE XIII. B. G., a forty-five year old white man, had had routine x-ray check-ups for the past seven years. However, at the time of his last x-ray an area of increased density had been observed at the left base. The patient was a rather nervous, jumpy individual whose general physical appearance was that of well-being. There was a noticeable huskiness of his voice. There was a lag to respiratory movements at the left base. The percussion note was flat up to the level of the eighth rib on the left, and the breath sounds were absent over the same area. No rales were heard. X-ray and fluoroscopic studies revealed an area of increased density at the left base confluent with the heart shadow. The left diaphragmatic shadow was obscured. The right lung was clear. Bronchoscopic studies revealed a normal right bronchial tree while the left stem bron-

chus was displaced forward with some narrowing of the bronchus but no fixation. At operation an ovoid mass was found lying in the sulcus posteriorly and it displaced the lower lobe forward and proximally. It was attached by a pedicle at the twelfth thoracic vertebra but did not enter the foramen. The mass weighed 1¼ pounds. Microscopic sections revealed the mass to be a neurofibroma. This man's earlier x-ray films had shown an area of increased density at the left base which had not been recognized.

Periodic examinations should include x-ray studies of the chest. The films should be studied by someone versed in diseases of the chest. There are none so blind as those who cannot recognize an object when it appears before their eyes.

Case xiv. R. C. was a fifty-two year old white man in whom a shadow was seen in x-ray of lung. He consulted a doctor because of numbness in his legs, heartburn and bloated feeling after eating, duration of symptoms one year. X-ray of chest made by the doctor revealed a round shadow about 3 cm. in diameter in the outer lower right lung field. There was an outer and central zone of increased density with a zone of decreased density in between. Physical examination was essentially negative. Fluoroscopic studies were confirmatory of the x-ray findings. Bacteriologic studies revealed no tubercle bacilli. Bronchoscopy revealed a mild degree of inflammation of the right lower lobe bronchus. At operation a globular mass about 3 cm. in diameter was removed together with the accompanying lobule of the lung. The mass was firm but on section it was found to have an area of liquefaction corresponding with the area of decreased density seen in the x-ray studies. The microscopic studies revealed the lesion to be a tuberculoma.

Similar shadows have been found to be carcinoma. We are of the opinion that all such lesions should be considered for surgical removal. Exceptions to this rule should be made only after due study and careful weighing of the dangers involved if the lesion eventually proves to be cancerous.

Case xv. N. F. P., a sixty-two year old white man, complained of shortness of breath. The patient had noted an increasing shortness of breath for the past three years. Recent x-ray studies revealed a mass in the right hilar area. The patient was somewhat overweight; he was short of breath and was cyanotic on exertion. The percussion note was resonant. There were numerous musical sounds heard especially on the right anteriorly and posteriorly. X-ray and fluoroscopic studies revealed some overinflation of the right lung field with an area of increased density about the right hilar area. The left hilar shadow was prominent. The sputum was negative for tubercle bacilli. Bronchoscopy revealed some narrowing of the right stem bronchus and a moderate degree of inflammation of the mucous membrane. There was no fixation. Impression was lymphadenitis with compression of the right stem bronchus. Antibiotics failed to give relief, and at operation a mass of lymph glands was found encircling and choking the bronchus. These were removed. The patient was relieved. Microscopic study revealed chronic lymphadenitis.

The symptoms in this case are very similar to those encountered in some cases of carcinoma. Rather than risk an error in diagnosis, exploratory thoracotomy was performed. The fibrosis within the lymph node was of such an extent that it is problematic if medication would have afforded relief. The mental and physical relief to the patient was ample reward. The risk was less than the dangers that accompany complete obstruction with infection distal to the obstruction.

Case xvi. M. M., a forty-six year old white woman, complained of arthritis. The patient consulted a doctor because of arthritic pains in her ankles. X-ray study revealed a mass in the right hilar area. The left hilar area was within the limits of normalcy. The physical findings were essentially normal except for a definite shortness of breath. Bronchoscopic studies revealed a moderate degree of inflammation in the right main stem bronchus without fixation. At operation a mass of large lymph glands encircled the right hilar area lying between the bronchi at each division. These were removed. The patient lost her arthritic pains. She received antibiotics. Microscopic studies revealed a chronic granuloma of the lymph nodes characteristic of sarcoid.

The similarity of the symptoms and physical and other findings between this case and some of the other cases leaves one with little desire to wait and see what will happen. Exploratory thoracotomy entails small risk as compared with the grief of a missed carcinoma.

We have presented a group of cases in which each patient presented some symptom or finding which was similar to the symptoms encountered in other patients afflicted with other diseases. Careful evaluation of all findings resulted in a planned program which proved to be effective in each case. The correlation of the symptoms, physical and laboratory findings with the living and anatomic and pathologic findings at the time of surgical intervention led to a rational understanding of the diseases in the various stages of their development.

SUMMARY

1. Many diseases involving the organs of the thorax may cause similar symptoms and other findings but there is generally some sign or clue that will lead to the correct diagnosis if the physician will only recognize it.

2. Assembly line medical practice is too impersonal. Each patient is a special and important person, to be dealt with as an individual.

3. Medicine and surgery as they are known today are the result of the efforts of our forefathers combined with our own efforts.

4. The astonishing advance in thoracic surgery has been brought about through the adaptation of procedures and medications to the peculiar anatomic and physiologic factors that are encountered within the thorax.

5. The study of the pathologic changes encountered in the living patient and the correlation of these findings in various cases have been of inestimable value to the diagnostician as well as to the surgeon.

Historical Development of Pulmonary Surgery*

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WHEN in the second half of the last century a new, important phase in the development of surgery dawned—when the introduction of anesthesia, of antisepsis and asepsis, new discoveries in anatomy and physiology, and developments in pathologic anatomy finally ushered in the "golden age of surgery"—operative technic was already established on a fairly sound basis. Only the endothoracic organs remained an area of which surgeons still fought shy.

True, there are cases reported by surgeons of the Middle Ages and the Renaissance in which resection of the pulmonary tissue was performed. Back in the thirteenth century Rolando of Salerno removed the gangrenous part of a lung that had prolapsed as a result of an injury to the thoracic wall. In the seventeenth century, under similar conditions, Fabricius Hildanus performed pulmonary resection with a red-hot iron. Yet in the numerous descriptions of thoracic and pulmonary injuries contained in the surgical literature of the Ancients and of the Middle Ages, there is not one mention of pneumothorax and seldom of subcutaneous emphysema. This is a sign that clinical observation in those days, although well advanced in other respects, still fell short when it came to studying intrapleural diseases, or else perhaps, was of no practical interest for lack of the means to treat such cases. Even the treatment of empyema—one of the outstanding achievements of the Alexandrine school of surgery—had so fallen into disrepute that Dupuytren (1777–1835), enterprising surgeon though he was, refused to allow this operation to be performed on himself.

Until the beginning of this century the approach to the problem of the traumatic open pneumothorax was not very different from what it had been at the time of the battle of Mantinea (362 B.C.) when Epaminondas, well aware of the fatal effect of the open pneumothorax, refused to remove the spear point from his breast until he learned that the Thebans had won the day. Even in the early days of the first World War the rule was still not to intervene in such cases, and the realization that it was enough to transform an open pneumothorax into a closed one to remove all immediate danger only slowly found acceptance.

Meanwhile the reticence shown toward open thoracotomy gave place to an important advancement which fifty years later was to become one of the cornerstones of the postoperative treatment of intrathoracic interventions.

In 1876 Bülau, a Hamburg physician, introduced the method of subaqueous drainage into the treatment of empyema. This he was induced to do by the unfavorable experiences encountered in performing open thoracotomy in children. His work shows that he had a clear conception and understanding of the dangers of the open pneumothorax, and from this time onward surgeons realized the need to reduce or eliminate these dangers during and after intrathoracic interventions.

The immediate effect of this realization was, admittedly, to hamper rather than to assist. The dangers of opening the pleura were grossly overestimated; and although in 1884 Krönlein, a Swiss surgeon, performed resection of a lung, many years went by before others followed suit. It was not until the turn of the century that isolated cases were reported (by Murphy, Tuffier, Heidenhain, Körte, Garré and Quincke, Lenhartz and others).

A turning-point in the history of intrathoracic surgery was marked by the publication in 1904 of Sauerbruch's experimental work entitled "The Pathology of the Open Pneumothorax and the Basic Principles of My Method of Eliminating It" ("Zur Pathologie des offenen Pneumothorax und die Grundlagen meines Verfahrens zu seiner Ausschaltung").

The history leading up to this study is an interesting one. Sauerbruch was at that time

* This article is part of the Mitchell Banks Memorial Lecture on "The Romance of Thoracic Surgery" delivered at the University of Liverpool on November 17, 1953.

assistant in Mikulicz' clinic in Breslau. For many years Mikulicz had set himself the aim of creating the necessary conditions for radical operation of esophageal carcinoma. The first important step in this direction seemed to him to be a method which would prevent collapse of the lung once the thoracic wall had been opened. Sauerbruch tried to produce increased pressure within the bronchi by means of a tightly fitting face mask but considered this method unphysiologic. More in accordance with the normal conditions of pulmonary function was an experiment in which the operating theatre was transformed into a sort of enlarged pleural space. The air pressure in the operating room was maintained by a constant vacuum at the negative values of the pleural space while the head of the patient, well isolated from the body, remained outside. Sauerbruch's pneumatic chamber, as this contraption was called, solved the problem—from the physiologic point of view—in ideal fashion.

However, even the most spacious and technically most perfect type of chamber (as built in the newly formed operating section of the Surgical Clinic at Munich University in 1921) broke down in practice: It was impossible to change the patient's position during operation without endangering the differential pressure; the surgeon and his assistants had very little room to move; the heat was almost unbearable; and, finally, it was extremely difficult to communicate satisfactorily with the anesthetist outside the chamber. For all these reasons the pneumatic chamber was abandoned, and today it is nothing more than an historical curio although it has since been resurrected in its original conception in the form of the "iron lung."

Meanwhile the system of high pressure breathing with a closely fitting face mask had long replaced the low pressure method. Despite the obvious drawbacks of the system, which inflated the stomach and made it impossible to draw off fluid contents of the bronchi, esophagus or stomach, Sauerbruch never discarded it. Today it seems hard to believe that he rejected the method of endotracheal insufflation although this was only in small part due to an unwillingness to learn. The decisive factor lay in the organization, or rather the lack of organization, in the field of anesthesia. Sauerbruch rejected on principle the idea of setting up anesthesia as a branch in its own right, detecting in this, as he thought—quite unjustifiably—a step which would split up surgery into a number of specialized branches. His voice was sufficiently influential in the continent to hold up a development there from which, in other countries, thoracic surgery was to benefit more than any other. The oral insertion of the endotracheal tube demanded technical experience and great concentration. It has done much to render the métier of professional anesthetist attractive to young doctors.

It should be mentioned in the interests of historical accuracy that controlled breathing, albeit in a primitive form, had already long been known to physiologists who kept their curarized animals alive by this means. The prerequisite conditions were clearly laid down in Meltzer's work, "The Respiratory Changes of the Intrathoracic Pressure," which appeared in 1892.

Inflation of the lungs during operation had already been performed in animal experiments by means of the intratracheal tube; however, to introduce this tube tracheotomy was necessary, and the combination of tracheotomy with intratracheal intervention was regarded as of questionable value because it rendered postoperative expectoration difficult. Today, when tracheotomy is sometimes performed precisely in order to clean out the bronchial passages, this argument strikes us as having no foundation; but at that time the idea of using tracheotomy to drain off secretions had not occurred to those concerned. The proposal to introduce the intratracheal tube via the mouth was first made by Auer and Meltzer in 1909.

Today, since "controlled respiration" has become a normal part of general anesthesia, it is hard to realize the air of mystery that still enshrouded it twenty years ago. This entailed a twofold drawback: On the one hand, the apparatus seemed so complicated and forbidding that few surgeons could really make friends with it; on the other hand, it was considered that even the most urgent of intrathoracic operations could not be performed without its aid.

For many decades the dangers of operative pneumothorax in man were undoubtedly grossly overestimated—at first for purely empiric reasons. Apparently no distinction was made between open and tension pneumothorax; otherwise it would soon have been discovered that only the latter is directly fatal.

When in the second half of the nineteenth century this method was given a trial in an attempt to solve problems of operative technic, the mistake was made (again in respect of the open pneumothorax) of applying observations made in animals directly to man. It was not until the second decade of this century that Duval, the French surgeon, pointed out the fundamentally different nature of the human and animal mediastina. Whereas in man the mediastinal pleura is sufficiently firm to prevent spontaneous tearing if only *one* pleural space is opened, in dogs due to the delicate nature of the mediastinal septum a unilateral open pneumothorax at once becomes an ambilateral one; as soon as the typical mediastinal flutter of the open pneumothorax sets in, the tenuous mediastinal pleura yields.

In thoracic surgery, Sauerbruch's method of differential pressure respiration had more psychologic than practical significance; it was easier for a surgeon to decide on an intrathoracic operation when he knew that he could operate "under cover" of this method. This was so despite the fact that in the first great phase of lung resection, historically speaking, the advantages of differential pressure were lost for two reasons: (1) despite many and varied experiments no reliable method of closing the bronchi had been found; (2) despite the fact that Bülau's drainage was known and widely used in the treatment of empyema it became an axiom that where the pleura was free the thorax must be hermetically sealed after every intrathoracic intervention. Patients subjected to lung resection, lobectomy or pneumonectomy in this orthodox fashion died from tension pneumothorax and severe pleural infection without any clear interpretation of the clinical symptoms emerging from the few case histories published. The understandable tendency to report only the successful cases led to regrettable delay. When in the early twenties Sauerbruch performed several lobectomies where the pleural space was free, with subsequent closure of the thoracic wall, the fact that the ensuing deaths were due to tension pneumothorax, so far as I can recall, was not so apparent as to have induced attempts to counter it. Due to insufficient knowledge of postoperative mechanical disorders, pathologists overlooked these findings at postmortem examination and usually gave pleural or mediastinal infection as the cause of death despite the fact that death in such cases was usually fairly sudden and violent. Since the mediastinal pleura was opened in suturing the hilus, the air under tension found its way into the mediastinum and so led to mediastinal emphysema. This fact escaped neither the clinician nor the pathologist, with the result that "mediastinal emphysema" was added to these reports as a contributory cause of death. From this the erroneous conclusion was drawn that the bronchial stump commonly retracted into the mediastinum and, where the stump sutures were not air-tight enough, provoked mediastinal emphysema.

From these failures and from a few successful cases of resection in which the pleura was found obliterated (Tuffier, Heidenhain, Morriston-Davies, Sauerbruch), the conclusion was drawn that *pleural obliteration must be obtained before risking lung resection.* Even if bronchial closure should then break down, the inevitable escape of air and infectious material would do no harm provided they passed into the site of operation which was separated from the rest of the pleural space and drained outward. The unreliability of every method of bronchial closure was not affected by Tiegel's subtle experiments. Here, also, the relevance of animal experiments was called in doubt; in the dog, for instance, it was found that every form of occlusion, even mass ligation of the hilus, was successful—a fact which rendered extensive pulmonary excision in the dog successful from very early on.

The first phase in the systematic performance of lung resection began at the start of the second decade of this century and ended with the publication of Brunn's paper in 1929. Various procedures were used in order to bring about protective pleural adhesions: extrapleural tamponade or plombage (Sauerbruch), endothoracic tamponade, mechanical damaging of the pleural endothelium "by poudrage" (J. Alexander) or by "scrubbing with dry gauze" (E. D. Churchill).

Generally speaking, *one* preparatory intervention proved insufficient. To produce obliterative adhesions in the region of the hilus repeated tamponade was usually necessary; in the operation which followed, the affected lobe was disengaged and its hilus either tightly tied with a rubber tube and left to spontaneous necrosis (Sauerbruch) or secured by several circular mass ligatures and immediately ampu-

tated (J. Alexander, E. D. Churchill). This was followed by tamponade of the large space resulting from the removal of the lobe. Extensive rib resection was unavoidable where this procedure was adopted. In order to accelerate the filling-out of the space several surgeons mobilized part of the neighboring healthy lobe by freeing it from its adhesions. The results obtained by this complicated procedure were not too bad, even judged by today's standards.

In 1930 we were able to report 32 cases of lobectomy in which the mortality rate was 10 per cent—roughly the average of what was then obtainable. True, these were all cases of bronchiectasis or multiple abscesses. The long time necessitated by the preparatory operations rendered this method impossible in treating cancer. Here, attempts at resection under cover of ahesions consisted of extrapleural freeing and ligation of the upper lobe; in the case of the lower lobe, exteriorization was performed similar to the Bloch-Mikulicz method for tumors of the colon. Not only was this method technically unsatisfactory, but also it cut across the basic principle of radical operation for malignant tumors since it did not permit of any high level separation of the hilar structures.

All methods of mass ligation, however, had one notable advantage, rapidity, which with the methods of anesthesia then current greatly contributed to the success of this operation. Even with the patient in Trendelenburg's position one had to reckon with the flow of suppurative bronchial secretion into healthy sections of the lung, the more so since breathing with the mask apparatus not only made it impossible to drain off the bronchi but also actually impeded any outflow by reason of the high pressure. The more quickly the hilus could be ligated, the less danger there was of the patient being suffocated by his own sputum or dying from aspiration pneumonia. One may state without exaggeration that the successful resections performed today became possible only with the final adoption of intratracheal insufflation and the possibility of bronchial drainage it afforded.

The advance toward a technic satisfactory from both surgical and anatomic points of view was made, it is true, not without some hesitation. This was partly because a clear conception of the hilar structures in the advanced stages of suppurative pulmonary diseases (which in those days were the only ones admitted for operation) was considerably complicated by the presence of secondary fibrosis and swollen lymph glands. An important intermediate stage was reached with Shenstone's construction of hilar tourniquets (1932); these greatly facilitated hemostasis following excision and avoided leaving dead tissue behind, which had been one of the great drawbacks of the technic of circular mass ligation. The feeling of security which Shenstone's instrument gave to surgeons was shown in the universal adoption of lobectomy in one stage as the method of choice in the surgical treatment of bronchiectasis. The drawbacks of the tourniquet method were twofold: Although it rendered more or less reliable hemostasis possible, it could not be relied on to close the bronchi satisfactorily. Moreover, in the majority of cases of malignant tumor radical excision by this means was not possible since a comparatively large tissue stump perforce remained in the hilus. It is significant that the first attempt at *individual ligation of the hilus* was undertaken in a case of cancer by E. D. Churchill in 1930:

"The tumour—a small squamous carcinoma—was too close to the hilum to permit the use of a tourniquet. After freeing the adhesions and dividing the pulmonary ligament, the artery and vein were separately ligated and the bronchus was cut across. My error was in not suturing the bronchus. Influenced by Sauerbruch's warning about mediastinal emphysema following bronchial suture, I tried to prevent it by placement of a tube from bronchial stump to the exterior. The patient died on the third postoperative day with confluent bronchopneumonia. The autopsy record reads: 'A small rubber tube-drain leads into the main (intermediate) bronchus through the surgical incision. There is a small thrombus found at the site of the ligature of the artery. The vein shows no thrombosis and both artery and vein are tightly closed at the point of the ligature.' "

Already before Shenstone published details of his tourniquet method Harold Brunn had written his work on lobectomy in cases in which the pleural space was free (1929). This represented the real turning point. The amazing results obtained by Brunn were not so much due, as he supposed, to the particular method of handling the hilus as to the institution of an intercostal subaqueous drainage which ensured

the removal of air and exudates and hence extension of the remaining lobe. The technic of total pneumonectomy developed along the same lines.

When in 1931 the problem of total pneumonectomy arose in the case of a 12 year old girl with diffuse bronchiectasis of the left lung, we decided to adopt the two-stage method, being more familiar with this procedure. As a matter of fact, the essential problem was not one of technic but of functional pathology. We had few qualms regarding the sudden loss of respiratory surface inherent in total pneumonectomy; traumatic surgery and collapsotherapy had already amply shown how well defunctionalization of an entire lung was tolerated. There was greater concern regarding the space left empty by removal of the lung. To be sure, several cases of agenesis of one lung had been reported in the literature and the authors had clearly explained the manner in which—by shifting of the mediastinum, elevation of the diaphragm and shrinkage of the corresponding thoracic cage—Nature solved this problem herself. The greatest fears, however, centered around the sudden occlusion of the main branch of the pulmonary artery. The observations made in pulmonary embolism lay clearly before us and we were well aware that under these conditions the occlusion of one of the main branches entailed a high mortality rate. The successful results obtained by Gluck and Biondi in animal experiments were not altogether applicable to man, for it was known from experience of pulmonary embolism that animal hearts deal with this condition far better than the human heart, presumably because of the greater reserve power.

The operation was performed in July, 1931. The lung hilus was ligated with a rubber tube and several silk sutures; fourteen days later the necrotic lung was sequestrated. Photographs taken six years later showed a healthy, well developed woman.

The success of this operation belied our misgivings. No emboli-like crisis occurred after occlusion of the left pulmonary artery; and although the rib resection was very limited, the remaining space was filled by displacement of the mediastinum and the heart, rising of the diaphragm and shrinkage of the thoracic wall.

The second successful pneumonectomy was performed in 1932 by Cameron Haight in Ann Arbor, Michigan, in a case of bronchiectasis. The technic was the same. Today, some twenty years after the operation, the patient still enjoys the best of health; a few years after the operation she even bore a child.

The third successful operation of this kind represented a twofold advance. It was performed by E. A. Graham of St. Louis in April, 1933, in a case of lung carcinoma, and was carried out in one session; true, breakdown of the bronchial closure rendered thoracoplasty necessary a few weeks later. The patient, a forty-eight year old doctor, is still alive and active in his profession today.

Graham made use of Harold Brunn's technic, the weak point of which lay in the closure of the bronchial stump.

The decisive step forward in improving technic was made by W. Rienhoff of Baltimore in July, 1933, when he operated upon a three and a half year old child with fibrosarcoma of the lung. He made a transpleural incision of the mediastinum, isolated the intramediastinal part of the right pulmonary artery, the superior and inferior pulmonary veins and the main bronchus, and ligated the three vessels; after complete excision of the lung he closed the stump of the main bronchus with separate sutures, reinforcing these by a flap of mediastinal pleura. Since the bronchus appeared to be successfully closed, drainage of the pleural space was dispensed with. The outcome justified this procedure. The postoperative course was free from complications. The child was drowned when bathing several years after the operation.

The principles of this technic were also adopted for lobectomy and segmental resection; since that time no essential changes in technic have taken place.

As can be seen, the path covered in the field of pulmonary resection was certainly not one of steady advance. Entire phases in this development today seem to us to have been superfluous and even misleading; conversely, minute technical details, as everywhere in surgery, have had the most tremendous repercussions. The time needed to bring them to the consciousness of surgeons and to persuade them to adopt them now seems to us to have been excessively long. In addition, much has taken place under the influence of factors lying outside the sphere of surgical endeavor. The disturbing increase

in malignant bronchial diseases, for instance, has done much to realize just that opportunity which radical pulmonary surgery so long lacked, i.e., the large number of patients requiring help and, with them, the growing number of doctors and surgeons ready to cooperate.

The initiative and for a long time even the practical performance in the operative treatment of pulmonary tuberculosis lay with the internists. In 1882 Forlanini had conceived the idea of the therapeutic pneumothorax; Brauer defined its indications; de Cerenville, a clinician from Lausanne, recommended collapse of the lung by means of local thoracoplasty as far back as 1885, and himself performed this operation.

Quincke, Lucius Spengler and again Brauer developed the method to the stage of complete rib excision; Mosler and de Cerenville attacked the tuberculous cavities directly; Jacobaeus introduced endoscopic pneumolysis; Baer proposed extrapleural pneumolysis with paraffin filling of the cavity thus obtained. Surgical opening of pulmonary abscesses was also first performed in systematic fashion by Brauer and Kiesling, both of them internists. It is an astounding fact—and certainly not one that reflects to their credit—that surgeons should have entered so late and so hesitatingly on a field of activity first prepared for them by other hands.

Few new developments have taken place since in the collapsotherapy of cavitarian tuberculosis. Artificial phrenic paralysis was used in animal experiments by Sauerbruch as long ago as 1905 and was subsequently introduced into the therapy of tuberculosis by Stürtz in 1911. Being an extremely simple method, it quickly achieved a popularity far exceeding its practical usefulness. Today, with equal extremism, it is rejected out of hand. Thoracoplasty underwent modification at the hands of Wilms and Sauerbruch, the result of which was to maintain a satisfactory mechanical effect while reducing the danger. This method, the paravertebral resection of the first to tenth ribs, is today considered obsolete. In passing posthumous judgment upon it people overlook the fact that the tuberculous patients presented to the surgeon thirty years ago usually suffered from an extensive disease; this meant that total collapse was necessary, but the poor general condition of the patients made any complete rib excision impossible. Only in later years, when operative indication was extended to limited lesions of the upper lobe, came the introduction of so-called apical thoracoplasty based on Brauer's principle of extensive rib resection.

Compression of the lung by means of fatty tissue (Tuffier) or paraffin (Baer), introduced following extrapleural pneumolysis, was practiced by few until 1932. Following up a suggestion of Mayer's of 1913, we recommended extrapleural pneumothorax. For ten years it enjoyed a popularity amounting to adulation. Then its drawbacks became so obvious that it was universally abandoned. Only now is its very limited field of usefulness beginning to emerge. The much despised paraffin filling of Baer proved better than its reputation and is now enjoying a resurrection in the form of other foreign bodies, as lucite-balls.

For the majority of surgeons these details of the indirect surgical treatment of pulmonary tuberculosis will be little more than historical reminiscences. Today excision so dominates the stage that there are many centers of thoracic surgery where thoracoplasty, pneumolysis and pneumothorax are complete rarities.

It is noteworthy that lung resection figures among the very first attempts at the surgical treatment of tuberculosis. In 1883 Block, a young Berlin surgeon, attempted excision of the focus on his cousin who was suffering from bilateral apical disease. The patient died during the operation. Postmortem examination showed that there was *no* tuberculosis. The surgeon committed suicide; a smug medical historian added: "and rightly so."

When after a long interval resections were again performed for tuberculosis, diagnosis was usually in error. Following technical advances in lobectomy and pneumonectomy, almost every surgeon active in this field at some time or other removed tuberculous foci in the erroneous belief that a tumor or bronchiectasis was present. Some of these cases (for instance, tuberculosis with secondary bronchiectasis) were "open" cases. In spite of the inevitable bacillary infection of the severed bronchus tuberculosis of the pleura or the thoracic wall seldom occurred. This removed the most powerful objections hitherto raised against systematic resection which was first advocated in 1943 by E. D. Churchill. However, excisional

therapy in tuberculosis would never have found such wide acceptance as it enjoys today had not the discovery of streptomycin and bacteriostatic chemotherapeutic agents largely eliminated the danger of postoperative tuberculous complications.

A variation of practical importance was segmental resection; this procedure is based on the fact—already known for many decades but hitherto little appreciated—that the segment and not the lobe represents the anatomic unit of the lung. Churchill and Belsey (1939) and Overholt (1947) may be regarded as the pioneers of this technic.

Indications for Pulmonary Resection

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THE advent of pulmonary resection has unquestionably revolutionized the *modus operandi* of lung diseases and today many patients suffering from primary malignancy, bronchiectasis, certain tuberculous lesions and numerous other chronic pulmonary conditions have an excellent chance of becoming completely well.

Formerly primary carcinoma of the lung was invariably fatai. To establish the diagnosis was to pronounce the patient's death sentence. Also presenting a hopeless problem were certain cases of pulmonary tuberculosis, especially those with bronchial occlusion. Bronchiectasis is another condition which had no satisfactory solution. Before the advent of bronchography it was frequently unrecognized and numerous cases were incorrectly diagnosed as unresolved pneumonia. Many of these patients were admitted to sanatoria with the mistaken diagnosis of pulmonary tuberculosis. In addition numerous patients with varied undiagnosed pulmonary conditions either recovered or succumbed as a result of progression of the disease. The autopsy findings in such cases tend to be those of advanced stages of the lesion.

However, with the successes obtained through surgical exploration and resection of lung tissue, associated with continued careful correlative teamwork with members of the allied specialties and laboratory services, knowledge relative to pulmonary diseases has increased appreciably and has made an understanding of the diagnosis and management of these disorders of general importance. Therefore, it has become advisable that the practicing physician, internist and pediatrician cooperate with the surgeon in the evaluation of patients with pulmonary disease, especially those who are not improving under a medical therapeutic regimen. In this way additional diagnostic procedures may be suggested and instituted; in some instances operable cases which may be benefited by surgery may be selected.

Fortunately in almost all instances pulmonary resection is an elective procedure, thus allowing ample time for adequate preoperative investigation of the patient by x-ray films of the chest, bronchograms, endoscopy and differential function tests. In this respect the thoracic surgeon may be far better informed concerning the nature, location and extent of the pathologic process than the surgeon who explores for internal disease in other regions of the body. However, if the cause of the disease process cannot be established, surgery should not be delayed. At exploration the true nature of the lesion can often be determined and a final decision as to the extent of resection necessary can be ascertained.

Pulmonary resection may be defined as the removal of an entire lung (pneumonectomy); the removal of one or more lobes of one or both lungs (lobectomy or bilobectomy of right middle and lower lobes); the excision of a bronchopulmonary segment of one or more lungs (segmental resection, unilateral or bilateral); or the resection of a portion of a lung smaller than a bronchopulmonary segment (local or wedge excision).

In this article the author attempts merely to enumerate the conditions which may require pulmonary resection. In addition, brief comments relative to the disease processes will be made. Obviously regardless of the type of disease being treated, cardiac disease, pulmonary insufficiency, advanced age, or a combination of factors that combine to form the so-called "poor surgical risk" may preclude surgical intervention. For more detailed discussion the reader is referred to subsequent articles in this symposium.

INDICATIONS FOR PULMONARY RESECTION

Removal of an entire lung or portion of a lung may be indicated in conditions in which the pulmonary tissue is so seriously diseased by neoplasm, infection, vascular damage or injury that its retention will either interfere with the well-being of the patient or cause his death. These conditions may be classified as follows:

Indications for Pulmonary Resection

I. Primary new growths of the lung
  A. Malignant
    1. Carcinoma
    2. Alveolar cell tumor
    3. Sarcoma
  B. Questionably malignant
    1. Bronchial adenoma
  C. Non-malignant
    1. Harmatoma
    2. Fibroma
    3. Chondroma
    4. Lipoma
    5. Myoblastoma
II. Metastatic "solitary new growths"
III. Lipoid pneumonia (paraffinoma)
IV. Chronic suppurative diseases
  A. Bronchiectasis
  B. Lung abscess
  C. Gangrene of the lung
V. Chronic pulmonary disease with varying degrees of atelectasis, pneumonitis and abscess formation (which do not clearly fall into the classification of either bronchiectasis or lung abscess)
  A. Chronic pneumonitis, cholesterol type
  B. Middle lobe syndrome
  C. Mucoid impaction of bronchi
  D. Spreading suppurative pneumonitis
VI. Tuberculosis
  A. Bronchial stenosis
  B. Destroyed lung or lobe
  C. Tuberculous bronchiectasis
  D. Tuberculoma
  E. Thoracoplasty failure
  F. Uncontrollable lower lobe disease
  G. Tension and thick-walled cavities
VII. Cystic diseases of the lung
  A. Non-parasitic cysts and cyst-like cavities
    1. Congenital pulmonary cyst
    2. Cystic bronchiectasis
    3. Epithelialized cavities following pulmonary suppuration
    4. Pneumatocele (localized alveolar or lobular ectasia)
    5. Emphysematous bullae
    6. Pulmonary blebs
    7. Intralobar bronchopulmonary sequestration
  B. Parasitic cysts
    1. Echinococcic (hydatid) cyst
VIII. Fungous infections
  A. Actinomycosis
  B. Nocordiosis
  C. Coccidiodomycosis
    1. Specific types of cavities
      a. Giant cavity
      b. Secondarily infected cavity
      c. Blocked cavity
    2. Rupture of cavity
    3. Non-expansible lung
    4. Hemoptysis
      a. Continued
      b. Severe
    5. Coccidioma, expanding lesion
    6. Failure of medical and collapse therapy
  D. Blastomycosis
  E. Histoplasmosis
  F. Aspergillosis
  G. Cryptococcosis
IX. Cavernous vascular lesions
  A. Arteriovenous fistula
  B. Capillary hemangioma
  C. Endothelioma
X. Traumatic injury to lung
  A. Large hematoma
  B. Expanding hematoma
  C. Profuse or continuing pulmonary hemorrhage
  D. Massive subcutaneous emphysema with tension pneumothorax following pneumonolysis

COMMENTS RELATIVE TO DISEASE PROCESSES

Primary New Growths of the Lung

Malignant. The principles involved in the removal of pulmonary tissue are simple and obvious. Applied to carcinoma the procedure is basically the same as that accepted for the treatment of gastric, colonic, rectal and mammary lesions of a similar nature. Today surgeons agree upon the removal of the entire organ which contains the cancerous lesion together with its regional lymphatics. Pneumonectomy with resection of mediastinal glands meet these basic surgical requirements, offering certain patients a chance of cure and palliation to others. In rare cases, notably peripheral tumors, cure can be obtained by simple lobectomy. Lobectomy is also the treatment of choice in patients with a low respiratory reserve, a poor cardiovascular system and

advanced age. In these cases the procedure should be considered palliative in nature. In patients with malignancy of the lung with mediastinal and chest wall extension, a palliative pneumonectomy may be justifiable since the associated secondary infection usually creates a most horrible situation and frequently precipitates the fatal outcome. During exploratory thoracotomy in a questionable case of lung carcinoma a competent pathologist will aid the surgeon in arriving at an accurate diagnosis. Segmental resection or lobectomy may be necessary to establish the diagnosis since a small piece of tissue removed from the periphery of the diseased lung need not be representative of the pathologic process.

Alveolar cell tumor: This rather uncommon neoplasm has been referred to as alveolar cell carcinoma, bronchiolar carcinoma and pulmonary adenomatosis. Ultimately unless resection is successful, the patient dies of asphyxia, pneumonia or metastases. Its treatment of choice is conservative pulmonary resection. This implies lobectomy. If the disease extends beyond the lobe with demonstrable lymph node metastases, then pneumonectomy with mediastinal node dissection is necessary.

Sarcoma of the lung: Primary sarcoma of the lung is a rare tumor and is treated by surgery similarly to carcinoma. The prognosis in these cases appears to be relatively more favorable than carcinoma. The diagnosis in these cases is only made after resection. They may not occur locally for long periods of time after resection.

TABLE 1*

SALIENT FEATURES OF BRONCHIAL ADENOMA AND BRONCHOGENIC CARCINOMA

	Bronchial Adenoma	Bronchogenic Carcinoma
Average age	37.4 yr.	53.2 yr.
Sex	Male to female—1:1	Male to female—3.8:1
Average duration of disease before surgery is instituted	5.9 yr.	11.3 mo.
Clinical picture	Hemorrhages, often profuse, with sudden onset and termination; intermittent episodes of pneumonitis with healthy intervals; bronchiectasis common	Hemorrhages, usually blood-streaked and continuous; progressive secondary pulmonary complaints without healthy intervals
X-ray findings	Tumor frequently not visible; only shadows incident to obstruction are seen	Tumor frequently is seen
Bronchoscopic picture	Often pedunculated, small, pink or yellowish in color; carina always sharp and mediastinum free; biopsy frequently followed by bleeding	Usually irregular, fungating, ulcerogranulomatous, non-pedunculated, gray or grayish-yellow; carina frequently blunted and mediastinum fixed; bleeding minimal
Metastases	Occasionally regional lymph nodes; rarely distant	Regional and distant metastases frequent
Amenability to surgical cure	Almost 100%	10%
Survival	Long duration	Short duration

* From Naclerio and Langer.[1]

Questionably Malignant New Growth. Bronchial adenoma, sometimes referred to as carcinoid, cylindroma, mixed tumor and endothelioma, accounts for approximately 80 per cent of the benign bronchogenic growths and is still the subject of much controversy. The indecision is due chiefly to accumulated evidence toward consideration of these tumors as potentially invasive and malignant. However, it is regarded by many as essentially benign. A review by Langer and the author of fifteen bronchial adenoma and 305 carcinoma patients treated by Overholt indicates that the conditions should be considered as different and essentially benign rather than as belonging to two grades or stages of the same neoplasm.[1] The salient differences are shown in Table 1.

Bronchoscopic removal was employed in the past for patients in whom there was no serious damage distal to the growth. However, this method of treatment has been practically

abandoned for the following reasons: local recurrences, danger of serious uncontrollable hemorrhage, inability to remove adequate amounts of tumor (the portion of the tumor outside the bronchus is often larger than the intraluminal portion) and in approximately 10 per cent of the cases there is evidence of metastases. The metastatic lesion may be localized to the regional or mediastinal lymph nodes or may be widespread throughout the body. Pulmonary resection is therefore indicated. Lobectomy is usually adequate except when the situation of the adenoma necessitates pneumonectomy.

Non-malignant New Growths. Less common tumors of the lung include harmtoma, fibroma, chondroma, osteochondroma, lipoma and myoblastoma. These tumors possess the features of benign tumors elsewhere in the body, i.e., they are well localized, usually round and lack the invasive properties of malignant tumors. Frequently they cannot be distinguished from the intrathoracic malignant tumors. Fortunately they are almost always near the lung surface and accessible for biopsy. Lobectomy is the treatment of choice in dealing with these neoplasms. In some instances local excision will suffice while in others segmental resection should be considered.

Metastatic Solitary New Growths

Metastatic tumors of the lung are extremely frequent and are associated with many diagnostic difficulties. Clinically and roentgenologically they may mimic tuberculosis, pneumoconiosis and primary tumor of the lung. However, "solitary" pulmonary metastases do occur and may be indistinguishable from a primary growth. Surgical removal of a solitary lung metastasis is indicated under certain conditions since there are in the literature enough reports of long survival of patients to make extirpation a rational method of treatment.[2] If the primary malignancy has been removed and has been under clinical control for a period of time and a solitary lung lesion is the only sign of metastatic disease, resection of lung by local excision, segmental repair or lobectomy may be justifiable. In rare instances pneumonectomy may be the treatment of choice.

Lipoid Pneumonia

This chronic disease, caused by ingestion of oil into the alveolar spaces and sometimes referred to as pulmonary paraffinoma, may simulate atypical pneumonia, lobar pneumonia, tuberculosis, neoplasm, infarction, a solitary metastatic lesion or bronchiectasis. It has been emphasized that pulmonary paraffinoma can mimic lung cancer clinically, radiographically, grossly at the operating table and is even mistakenly called cancer on frozen section.[3] In these cases needless pneumonectomy is performed when lobectomy is the treatment of choice. According to Davis et al.[4] "the importance of this disease should not be minimized because it is often disabling." In addition they mention that this disease may sometimes be fatal.

Chronic Suppurative Diseases

Bronchiectasis. This disease may involve a whole lung, one lobe, two or more lobes, a bronchopulmonary segment or, more frequently, multiple bronchopulmonary segments in both lungs. Surgical removal of the affected part constitutes the only rational treatment. In properly selected cases cure is practically certain. Pneumonectomy is indicated when there is extensive involvement of all lobes in one lung. When the lesions are limited to one or two lobes, lobectomy and bilobectomy of right middle and lower lobes should be performed. Patients with bilateral disease are candidates for palliation or cure, with the use of bilateral segmental pulmonary resection performed in two stages.[5]

Lung Abscess and Pulmonary Gangrene. It is extremely difficult and sometimes impossible to make a differential diagnosis between lung abscess and pulmonary gangrene. In either case one is dealing with destruction of tissue and for this reason there is a tendency to consider the two conditions together. The term pulmonary gangrene is ordinarily applied to a massive necrosis of lung tissue without tendency to localization. This disorder is much less frequent since the advent of antibiotic agents. Secondary infection of the contents of a simple purulent abscess may lead to spreading gangrene. On the other hand, some cases of gangrene of the lung become limited and after expectoration of necrotic tissue, the anaerobic infection subsides and a simple abscess remains.

Satisfactory results obtained today in the treatment of lung abscess are accounted for by the more prompt application of surgery and, particularly, the utilization of lobectomy.

Indications for surgical excision in the treatment of this condition are: (1) when the disease is chronic with associated lung damage such as fibrosis, bronchiectasis, atelectasis (the chronicity of the case constitutes the most frequent indication); (2) when multiple cavities exist in one or more lobes; (3) when there is persistent disease following drainage operations; (4) when a bronchogenic neoplasm is suspected as an underlying cause; (5) when the lung abscess is associated with a retained foreign body; and (6) when the condition is found in children. Postoperative care of drainage procedures in children is notoriously difficult. In addition, many develop bronchiectasis following drainage. On the other hand, lobectomy is well tolerated by children.

Chronic Pulmonary Disease with Varying Degrees of Atelectasis, Pneumonitis, Abscess and Bronchiectasis Formation

Chronic Pneumonitis, Cholesterol Type. The descriptive term "chronic pneumonitis, cholesterol type," has been used to designate a clinical entity variously described for many years as a subacute chronic interstitial or fibrous pneumonia.[6] This condition is characterized by the deposit within the pulmonary parenchyma of high concentration of cholesteral and cholesterol esters. In the majority of these cases a preoperative diagnosis of cancer of the lung is made. Since the pneumonic process usually involves the entire lobe, lobectomy usually suffices in effecting a cure.[7]

Middle Lobe Syndrome. This disease entity, a middle lobe atelectasis of non-tuberculous origin with suppurative changes, has been described by Graham et al.[8] Inflammatory processes involving the middle lobe and on occasion the lower or upper lobes on the right side may result in enlargement of the peribronchial lymph nodes. Since the lymph nodes are so arranged about the middle lobe bronchus, only moderate enlargement of them will cause complete bronchial occlusion resulting in atelectasis. Secondary infection will invariably lead to pneumonitis, lung abscess or bronchiectasis. In these cases a middle lobe lobectomy is the only satisfactory method of treatment.

Mucoid Impaction of the Bronchi. This descriptive terminology designates a disease entity found in patients with an underlying condition of asthma or chronic constrictive bronchitis. The mucoid impaction of the bronchi results from a localized accumulation of inspissated mucus in the bronchi. This condition may simulate neoplasm, abscess and tuberculosis clinically and roentgenologically. According to Shaw[9] who has described this entity, indications for resection are: (1) persistence of suppuration with destruction of mucus; (2) repeated hemoptyses from the associated cystic bronchiectasis; and (3) the necessity of ruling out neoplasm when the diagnosis is not certain.

Spreading Suppurative Pneumonitis. This condition has been described by Sellors et al.[10] as a non-specific inflammation with cavity formation, in some instances leading to death from toxemia but more often to permanent damage to the lung.[6] They emphasize that "radical excision of a lung or lobe may be the only method of saving the life of certain patients; in others whose life is not in immediate danger, it may be the only method of dealing with the lesion."

Tuberculosis

In pulmonary tuberculosis the use of potent antimicrobial agents in combination with surgical therapy has rendered previously dangerous procedures relatively safe. At the present time most thoracic surgeons agree that the indications for pulmonary resection include: (1) bronchial stenosis; (2) destroyed lung or lobe; (3) tuberculous bronchiectasis; (4) tuberculoma; (5) thoracoplasty failure; (6) uncontrollable lower lobe disease; and (7) tension and thick-walled cavities.

Indications for resection are debatable in patients who have either a small non-cavitary fibrocaseous residuum or small closed cavities. In these cases the "Snip operation" or local excision method of treatment has been advocated.[11] Further trial is necessary before an adequate evaluation of the procedure can be made.

Cystic Diseases of the Lung

These diseases are of special interest because the term "cystic diseases of the lung" has been used to designate a wide variety of pathologic entities. The lesions involved in this group are: congenital pulmonary cyst, cystic bronchiectasis, epithelialized cavities following pulmonary suppuration, pneumatocele (localized alveolar or lobular ectasis), chronic interstitial pneu-

monitis with emphysema, emphysematous bullae, pulmonary blebs and echinococcic (hydatid) cyst. Intralobar bronchopulmonary sequestration may be conveniently added to this group.

The presence or absence of an epithelial lining in these lesions controls the symptomatology and for the most part dictates the treatment. Epithelialized cysts are best treated by pulmonary resection similarly to bronchiectasis and chronic abscess.

Pulmonary cysts not lined with epithelium, i.e., emphysematous blebs and bullae, are not generally understood. A thorough knowledge of the existing condition and associated alteration in the physiodynamics of the chest is necessary in planning the best type of therapy. In some cases pulmonary blebs and bullae, even when large, can be asymptomatic and frequently will disappear spontaneously. These patients are obviously not candidates for surgery. In other cases in which there is obstruction to the egress of air in the bronchus (check valve mechanism) the cyst will balloon out and acquire large dimensions, in extreme cases filling the larger portion of both pleural cavities and causing incapacitating dyspnea. Until a few years ago there had been no satisfactory treatment for this condition. Head and Avery[12] reported on fifteen patients with large emphysematous bullae and two with bronchogenic cysts who were greatly benefited by intracavitary (Monaldi) suction. Others have experienced good results with lobectomy and pneumonectomy. Langer and the author[13] described the use of local excision technic with excellent results. This procedure is contraindicated, however, in the presence of an epithelial lining. In cases in which a low respiratory reserve exists the use of intracavitary suction may prepare the patient for thoracic exploration and definitive surgical therapy.

In intralobar bronchopulmonary sequestration a lesion exists when there is essentially a cystic condition in a segment of a lower lobe; supplied by an anomalous artery arising from the lower thoracic or upper abdominal aorta. The treatment of choice in these cases is either segmental resection or lobectomy. The author has had experiences with three such cases, one having been reported in 1950.[5]

Pulmonary hydatid disease may also constitute an indication for pulmonary resection. When spontaneous expectoration and evacuation is present, healing may occur without complications. In patients in whom secondary infection of the cyst with abscess formation is seen, the condition should be treated as a pulmonary abscess. Lobectomy offers the only chance for cure when repeated hemoptysis occurs and may be considered in the presence of many scattered cysts in one lobe.

Fungous Infections

Resection may be the therapy of choice in selected chronic localized pulmonary fungous infections that remain after adequate medical treatment has been instituted.

Actinomycosis. Surgery is reserved for those cases with irreversible damage to the lung. This damage may be based in part on secondary pyogenic invaders. Pleural contamination invariably requires surgical damage, but pulmonary lesions usually drain through the bronchi. The mortality in untreated pulmonary actinomycosis is not known but may approach 90 per cent. This has been materially reduced but not eliminated by sulfonamide-penicillin-iodide therapy, supplemented by surgical excision of one or more lobes.[14]

Nocordiosis. In this condition pulmonary resection may be required when the differential diagnosis from neoplasm remains in doubt.[15]

Coccidiodomycosis. Most patients with pulmonary coccidiodomycosis are asymptomatic. Some may have moderate to severe symptoms. Frequently some patients with moderate to extensive lung infiltrations become asymptomatic but may harbor a thin wall cavity which persists for months and years. If a patient has persistent cough and associated expectoration of sputum, the cavity area should be removed by wedge resection, segmental resection or lobectomy.[14] Cotton outlines the indications for resection as follows:[16] (1) Specific types of cavities: giant cavity, secondarily infected cavity and blocked cavity; (2) rupture of cavity; (3) non-expansible lung; (4) hemoptysis, continued and severe; (5) coccidioma, expanding lesion; (6) failure of medical and collapse therapy.

Blastomycosis. Buechner et al.[17] state that the management of blastomycosis should simulate that of pulmonary tuberculosis. They suggest that the combined use of drug therapy (diamidines, iodides and vaccine [blastomycin]) and resection might offer more favorable results in pulmonary blastomycosis, just as

streptomycin and para-aminosalicylic acid combined with surgery have improved the prognosis of tuberculosis.

Recent discovery of the effectiveness of stilbamidine in the treatment of pulmonary blastomycosis has apparently altered the prognosis of this disease. Acree et al.,[18] on the basis of short-term observations, state that the prognosis of pulmonary blastomycosis is excellent when treated with 2-hydroxystilbamidine followed by surgical resection if necessary.

Histoplasmosis. As yet there is no specific treatment for histoplasmosis. However, in case of localized reinfection typed histoplasmosis, surgical resection is curative.[14] Hodgson et al.[19] reported two cases in which resection had been performed for cavitational disease. According to Puckett[20] pulmonary histoplasmosis is a common disease entity which achieves surgical importance mainly because of its propensity to leave residual foci that mimic tuberculosis, neoplasm or other diseases.

Aspergillosis. In bronchopulmonary aspergillosis localized abscesses should be drained and granulomatous areas excised if possible. Gerstl et al.[21] and Yesner and Hurwitz[22] had success with pulmonary resection for localized manifestations of this disease.

Cryptococcosis. Baker[23] refers to three cases of pulmonary cryptococcosis treated successfully by resection. Dormer et al.[24] reported a case in a twelve year old boy treated successfully by pneumonectomy. Postoperatively meningeal symptoms developed and positive inoculation in the guinea pig was obtained from the spinal fluid. These symptoms responded to large doses of iodides and the patient was discharged two weeks later. Froio and Bailey,[25] in reporting a successful cure, emphasized that pulmonary cryptococcosis without meningeal involvement is unusual, and suggest that if the disease is local and can be diagnosed and removed before meningeal spread has occurred, the patient may be cured. It should be mentioned that the primary pulmonary lesion may be inconsequential or never detected, and the patient appears with a brain or meningeal lesion.

Cavernous Vascular Lesions

These lesions are large and complex communications between the pulmonary arteries and veins. Synonyms and related terms of these lesions are arteriovenous fistula (varix), arteriovenous aneurysm, hemangiona and telangiectasis.[26] The presence of an arteriovenous fistula with or without symptoms is sufficient indication for surgical treatment. Treatment of this condition consists of surgical interruption of the fistula or excision of the vascular mass. Because of the difficulties associated with ligating the communication between the artery and the vein, local or segmental resection is the procedure of choice. In most patients, however, lobectomy or pneumonectomy is necessary because of the size and location of the vascular channels. Maier[27] has pointed out that because of the possibilities of associated vascular anomalies, one should be certain that adequate channels remain for the return of blood to the left side of the heart.

Capillary hemangioma and endothelioma are rare in the lungs and when they occur have the characteristics of similar tumors elsewhere. In these cases segmental resection may be the treatment of choice.[26]

Traumatic Injury to Lung

In the case of perforating or penetrating injuries to the lung conservative measures are usually sufficient. Occasionally, however, it is imperative to enter the chest whereupon segmental repair and local excision may suffice. If a hematoma exists which is of sufficient size to involve an entire lobe, lobectomy is indicated. In the event of an expanding hematoma which threatens to perforate, either lobectomy or pneumonectomy is advisable depending upon the location of the hematoma.[28] Occasionally damage may be so extensive that pneumonectomy offers the only hope of controlling hemorrhage and shock. Emergency thoracotomy must be performed in some instances of closed pneumonolysis when early massive subcutaneous emphysema with tension pneumothorax or profuse hemorrhage into the pleural cavity occurs. Treatment may then consist of segmental repair, local excision or resection.

SUMMARY

1. An outline of conditions which may require pulmonary resection is presented.

2. Serious cardiac disease, borderline ventilatory function, advanced age or a combination of factors that combine to form the so-called "poor surgical risk" may preclude surgical intervention.

3. Brief comments relative to the disease processes outlined are made.

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Principles of Pulmonary Resection

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IN recent years intrathoracic surgery has become so safe that excision of a pulmonary lesion is usually the indicated treatment when surgical therapy is contemplated. Resection has reached this preferential position as a result of improved technical methods, the wide spectrum of protection afforded by antibiotics, the improvement in anesthesia that permits the pleural cavity to be open for long periods without hazard, the development of procedures to determine ventilatory function and finally the better understanding of pre- and postoperative management. These have provided the foundation on which thoracic surgery rapidly grew to maturity, one of the most spectacular records in the annals of surgical history.

Before the latter part of the nineteenth century successful pulmonary resections were few—for the most part, fortuitous—and their records were poorly documented. However, with the introduction of asepsis in surgery the possibilities of pulmonary resection were explored both clinically and experimentally, and by 1920 somewhat less than 100 resections had been reported.

A more than 50 per cent mortality and rather indifferent results stimulated a second period of experimentation, and during the ten years between 1920 and 1930 much new information was gathered and previous work clarified.[1] These experiments may be summarized as follows: (1) The advantages of individual isolation and division of hilar structures were demonstrated. (2) A number of safe and simple methods for closure of the bronchial stump were devised. (3) The fate of the large intrapleural cavity remaining after pneumonectomy was determined: It was found to fill with variable amounts of fluid, and its size to diminish by elevation of the diaphragm, retraction of the chest wall, shift of the mediastinal contents toward the operated side and expansion of the remaining lung. (4) The compensatory enlargement of the remaining lung after pneumonectomy was established as being primarily the result of dilation of the atria and the terminal air sacs. (5) Ligation and division of the pulmonary artery were proved to cause little or no change in the blood pressure or pulse rate; as a rule, pneumonectomy did not alter the heart action unless there was undue traction upon the hilar structures, which might result in sudden and severe alterations in the cardiac efficiency. (6) After pneumonectomy it was found that there was a temporary increase in the alveolar CO_2, a fall in the alveolar oxygen, a slight increase in the CO_2 content of the blood and a marked decrease in blood oxygen; compensatory changes of a circulatory nature resulted in an increase in blood flow and pulse volume during the temporary decrease in total lung volume. (7) Finally, animals, up to a year after operation, were found to show no appreciable enlargement of the heart, although occasionally hypertrophy of the right ventricle seemed definite. Animals were normally active, free from dyspnea, and healthy.

As a result of these findings the period from 1930 to 1940 serves as another brilliant example of the successful clinical application of methods and principles originally conceived and developed in the experimental laboratory.

MANAGEMENT OF PATIENTS

Every effort should be made to establish a correct preoperative diagnosis since often the operative treatment is determined by the type of disease. However, in view of the safety of exploratory thoracotomy the inability to make a diagnosis should not cause delay in treatment. Unfortunately, one of the most common errors today is that of wasting precious time in the hope of arriving at a diagnosis, which often can be made only after removal of the lesion.

In planning pulmonary resection, as in any major surgical operation, the patient's general condition must first be carefully evaluated, preferably by collaboration between internist and surgeon.

Special attention must be paid to the cardiovascular system, which is subjected to an unusual burden during and after most intrathoracic procedures. The heart with coronary artery disease, often well compensated under normal circumstances, is particularly vulnerable and, although usually no contraindication to operation, it does require a guarded prognosis, particularly after pneumonectomy.

Just as important is a careful evaluation of the ventilatory function, to be sure that the contralateral or uninvolved lung will provide adequate oxygenation both during and after operation. While in a patient with carcinoma a liberal attitude should determine operability, the tuberculous patient must be critically analyzed because alternative methods of therapy may be available. Moreover, where extensive disease is found in one side, it must be assumed that at some time the process has been bilateral.

For instance, a young woman of twenty-five years was considered for correction of a coarctation of the aorta. Her problem was complicated by bilateral tuberculosis of nine years' duration, for which she had received bilateral pneumothorax treatment until two years previously, when the right pneumothorax was discontinued. A minimal pneumothorax on the left had been maintained. The problem was whether or not the ventilatory function of the right lung would be adequate while the left chest was open during the coarctation correction. The chest x-ray revealed minimal collapse of the left upper lobe, obliteration of the right costophrenic sulcus, and some retraction of mediastinal structures into the right chest. Partial bronchial stenosis of the right main stem bronchus was observed at bronchoscopy. Bronchosperometry revealed 92.3 per cent of total oxygen consumption on the left but only 7.7 per cent on the right. On the basis of these findings it was decided that collapse of the left lung might be disastrous and precluded operative repair of the coarctation.

Other systems that may be the cause of a patient's complaints should be investigated. In the tuberculous patient extrapulmonary tuberculosis must be excluded since this complication not only adversely affects the prognosis but also may contraindicate surgical treatment of the pulmonary lesion. If lung tumor is suspected, every effort should be made to exclude the possibility of its being a metastasis from a primary tumor in some other region.

For instance, recently a patient was referred for removal of a lesion in the upper lobe of the right lung. She was anemic (hemoglobin of 7.5 gm., red blood count of 2.7 million)—a rather unusual finding in primary carcinoma unless associated with infection or metastasis. Further investigation revealed persistent occult blood in the stool. Only after a second gastrointestinal x-ray examination was a defect seen in the second portion of the duodenum. At exploratory laparotomy carcinoma of the duodenum with several small liver metastases was found.

PREOPERATIVE PREPARATION

In the preparation of patients for pulmonary resection attention should be paid not only to their local problem but also to their general condition.

In the immediate preoperative management the patient must be prepared both physically and psychologically for a pulmonary resection. In any chest operation the patient should be assured of a successful outcome since removal of the lung is still considered by many to be extremely hazardous. He should be instructed in the importance of forced coughing, periodic deep breathing and frequent exercise of arms and legs. He should be informed that procedures such as blood transfusions, intravenous fluid administration, and the use of oxygen are routine postoperative measures. (To the uninformed patient an oxygen tent may indicate a hopeless situation.) For a particularly apprehensive person consultation with a patient who has already recovered from an operation and who is about to leave the hospital may be of value.

Antibiotics should be routinely given, the type depending upon the disease being treated. For the patient producing considerable sputum a prolonged preoperative course may be necessary to reduce his sputum to a minimum, not only to ensure a more satisfactory anesthesia but also to prevent postoperative atelectasis and pneumonia. A combination of dihydrostreptomycin and penicillin affords a wide spectrum of protection; as a rule it should be given at least forty-eight hours before operation. Before administration of any antibiotic every effort should be made to elicit a history of sensitivity and, even though sensitivity is

doubtful, appropriate steps should be taken to disprove it. For instance, recently a patient with a "coin" lesion in the left lower lobe was being considered for surgical treatment. He recalled that on one occasion about two years previously he had felt faint after having had an injection of penicillin, but that a year later several injections had been well tolerated. He was given a combination of penicillin and dihydrostreptomycin in the preoperative preparation, whereupon he promptly lost consciousness, became incontinent, pulseless and cyanotic, a typical picture of anaphylactic shock. Fortunately he recovered rather promptly, but subsequent electrocardiograms revealed changes in the T waves which were interpreted as coronary insufficiency requiring postponement of treatment. Although such a severe reaction is most unusual, it might have been avoided by using test doses to determine whether a true sensitivity existed.

As a rule digitalization should be used for those patients who have had recent heart failure or who are fibrillating. Vitamins should be given routinely pre- and postoperatively. The bowels should be relatively empty at the time of operation to minimize postoperative abdominal distention.

ANESTHESIA

Anestheologists have contributed much to the development of both agents and methods of anesthesia that now permit the surgeon to operate safely and unhurriedly while both pleural cavities are open. The responsibilities of the anestheologist have also been broadened. From his examination of the patient he determines the preoperative medication and type of anesthesia, directs the administration of the kind and amount of fluid during the operation, and chooses the sedation for the immediate postoperative period. In this way during the operation not only is the patient maintained in the best physiologic state, but also the surgeon may give his undivided attention to the operative procedure.

Generally speaking the anesthesia of choice is one that provides the highest percentage of oxygen compatible with adequate anesthesia, namely, ether, cyclopropane and nitrous oxide, either alone or in combination. Preliminary induction with intravenous pentothal® has proved a great boon to both patient and anesthetist. Ether is indicated for those patients who have exhibited cardiac irritability and arrythmias. Cyclopropane, from which recovery is rapid, is desirable in patients with considerable bronchial secretion so that the cough reflex may be quickly re-established. Nitrous oxide, as a rule, is used in combination with curare. Special drugs should always be on hand for use in special situations: atropine to abolish an undesirable vagal reflex, procaine used locally to eliminate reflex mechanisms, procaine amide to correct irregularities in the irritable heart, nor-epinephrine and neosynephrine to combat peripheral vasodilatation, oubain for rapid digitalization and curare in combination with controlled ventilation for muscle relaxation.

Intratracheal intubation provides a patent airway, complete control of respiratory movements and a means for satisfactory aspiration of the tracheobronchial tree. To provide the maximum blood oxygenation while the chest is open, the lung should be kept as fully inflated as is compatible with satisfactory exposure for the surgeon. Periodically the lung should be completely expanded and the airway aspirated so as to minimize postoperative atelectasis and pneumonia.

TECHNIC

Some general considerations apply to any type of pulmonary resection. Generally speaking the operative approaches most commonly used are the posterolateral, anterior and posterior. The particular choice is often determined by the type of operation or by the disease being treated. For instance, wide exposure of the mediastinum is necessary in the patient with carcinoma in order to facilitate adequate resection of the mediastinal lymph nodes, whereas this is not so important in the tuberculous patient. Although the posterolateral approach affords excellent exposure, on occasion it is poorly tolerated by the patient and, as pointed out by Beecher,[2] it compromises the ventilatory exchange. This complication is avoided by using either a posterior or an anterior approach. As emphasized by Overholt, the posterior approach with the patient in the face-down position reduces the danger of his bronchial contents spilling into the contralateral lung field.

The importance of maintaining the blood volume during the operation cannot be overemphasized. It is wise to begin the administra-

tion of blood when the skin incision is made, so as to provide gradual blood replacement and avoid the necessity for rapid infusion. In this way, during pneumonectomy abrupt and serious changes in blood pressure at the time of the division of the pulmonary artery may be minimized. After the division of the pulmonary artery the administration of large amounts of blood is inadvisable since at that time there is a sudden alteration of the cardiovascular dynamics which must be compensated for.

The necessity for individual isolation, ligation and division of the hilar structures needs little comment; mass occlusion is never necessary. Since traction on the pulmonary artery and bronchus may result in a sudden precipitous reflex drop in blood pressure, their isolation should be carried out as gently as possible. Sensitive reflex mechanisms frequently show themselves by a change in the heart rate, often a bradycardia, for which atropine parenterally or novocain locally is indicated. In the event of a reflex precipitous fall in blood pressure nor-epinephrine may dramatically restore the blood pressure. When the premonitory signs of cardiovascular dysfunction develop, manipulation and dissection should be stopped, and retractors should be removed until a normal and satisfactory heart action is re-established.

Anatomic variations of the pulmonary veins are not uncommon. Before division of a vein in any resection less than a pneumonectomy, the amount of lung it drains must be accurately determined.

Certain fundamentals are common to all satisfactory methods for closure of the bronchus. First, any type of crushing clamp should not be applied to the part of the bronchus that is to be closed. The soft membranous portion of the bronchus should be approximated to the semi-rigid cartilaginous portion by loosely tied sutures so as to prevent their tearing through the soft membranous wall. Equally important is the covering of the bronchial stump with pleura, whether it be an attached or a free pleural graft, so as to provide the ideal condition for rapid wound healing. Serum trapped between the covering and the stump is quickly replaced by granulation tissue, which in turn leads to early fibrosis and a firm closure of the end of the bronchus.

The use of tubes to drain the pleural cavity is determined by the type of operation. Following pneumonectomy, a tube may be used as a temporary safety measure; it should be kept occluded except when it is desirable to alter the intrapleural pressure by either the removal or the introduction of air. With lesser resections it is wise to use two tubes: one placed inferiorly for drainage of blood and serum, and the other placed superiorly for removal of air so that early and complete re-expansion of the remaining lung is facilitated.

A word should be said about the gentle transference of the patient from the operating table to the bed. To avoid a sudden drop in blood pressure due to sudden changes in position, all handling and repositioning should be done slowly and carefully.

POSTOPERATIVE CARE

Vigilant observation of the patient during the early postoperative hours is of utmost importance. It is during this time that serious or fatal complications of shock incident to change in position of the patient, cardiac standstill for reasons often undetermined, or tension pneumothorax may occur without warning. The immediate recognition and treatment of their complications is best achieved in a recovery area, fully equipped to cope with any resuscitive emergency, and staffed by experienced personnel under the direction of the anesthesiologist. Only with some such arrangement can the highest standards of patient care and efficiency be maintained.

Following any partial excision of a lung, the tubes inserted at the time of operation should be connected to a system of suction drainage as soon as it is practicable. As an aid in maintaining patency the tubes may be periodically "milked" toward the chest so as to dislodge any clot that may lie against the open end. When drainage stops, which usually is within seventy-two hours postoperatively, the tubes should be removed. Following pneumonectomy the tube (used not for drainage but only to facilitate correction of undesirable intrapleural pressures) may be safely removed within forty-eight hours unless a bronchial leak persists.

Enough sedation should be given to ensure the patient's comfort. If quantities sufficient to depress the cough reflex are required, forced coughing should be begun during the first twenty-four hours after operation and continued for the next five to seven days. Patients do far better in cleaning their bronchial tree

if the periods of forced coughing are spaced after sedation and are combined with changes of position and with compression of chest wall either manually or by means of a heavy towel wrapped around the thorax.

Bronchial aspiration is rarely necessary after the patient has recovered from anesthesia if close attention is paid to simple measures for maintaining a dry tracheobronchial tree. On occasion abdominal distention may prove distressing; it is undesirable since it reduces ventilatory function. Frequent turning of the patient, restriction of fluid and food, judicious use of small enemas, and early ambulation will usually prove effective.

Daily roentgenograms for the first four or five days provide necessary information concerning the unoperated lung, the position of the mediastinum, and the re-expansion of the remaining lung in cases of partial resection.

INDICATIONS FOR PULMONARY RESECTION IN SPECIFIC DISEASES

In bronchiectasis, in chronic lung abscess and in localized chronic, non-suppurative pneumonitis a good result may be expected to follow surgical removal; while, by contrast, conservative treatment leads to a high morbidity. In these diseases every effort should be made to follow Churchill's[3] dictum of preserving the maximum amount of normal lung tissue. Particularly in bronchiectasis, which often involves more than one lobe, this is possible only after accurate localization of the involved lung by bronchography, supplemented on occasion by tomographic roentgen studies. In patients with bilateral bronchiectasis ventilatory function studies may be indicated to be sure that open thoracotomy can be safely performed, although, if both upper lobes are free of disease and the patient is not dyspneic, resection will be well tolerated. In bilateral bronchiectasis, it is wise to delay the second operation on the opposite side for at least a year.[4]

It is in this group of diseases that every effort should be made to reduce the amount of sputum to a minimum so as to lessen the possibility of aspiration during the anesthesia. This can usually be done by bedrest, postural drainage, antibiotics and on occasion bronchoscopic aspiration to remove a mucous plug that is preventing satisfactory drainage.

Operative removal should be designed in a conservative pattern. These are the cases in which excision of segmental divisions of the lobe finds its greatest usefulness. It must be emphasized that the satisfactory use of segmental resection depends upon a sound knowledge of the segmental anatomy of the lung and the accurate preoperative localization of the disease.[5–7]

Brief comment should be made of local excision of single pyogenic abscess of the lung. In a small group of cases it has been found that local excision of primary lung abscess during the subacute phase is an ideal procedure since it retains the maximum amount of normal lung tissue and is well tolerated by the patient.[8] Briefly, excision consists of identifying the capsule of the lung abscess and using the capsule as the border of dissection from the normal lung tissue. Since most lung abscesses involve a true bronchovascular segment of the lung, the excision can be easily carried out with surprisingly little bleeding. It is necessary, of course, to identify and ligate the primary vessels and bronchus leading to the abscess and, in addition, the bronchial stump should be covered with a free pleural graft.

TUBERCULOSIS

Evaluation of the tuberculous patient for excisional surgery must be exceedingly critical since usually alternative methods of therapy are available. However, up to the present, the results of excisional surgery have been so satisfactory that it is now the preferred treatment when surgery is indicated. At present, the more generally accepted indications for excisional therapy are as follows: (1) postthoracoplasty failures; (2) bronchial stenosis; (3) tuberculoma; (4) firm, thick-walled, fibrous cavities; (5) chronic disease associated with bronchiectasis and large-tension cavities; (6) destroyed lungs; (7) localized disease resistant to conservative therapy.

In planning excisional therapy the proper preoperative management and timing of the operation are fully as important as the type of surgery. It is essential to give the maximum protection with antibiotic therapy, and whenever possible the operation should be performed while the antibiotics are still effective. Excisional therapy must be considered as only one phase of any therapeutic plan and as such must be preceded and followed by conservative treatment.

CARCINOMA

Because surgical removal of a carcinoma is the best therapy available at the present time (ample statistics having revealed the inadequacy of x-ray therapy), a liberal attitude should determine operability. If the patient has not noticed dyspnea in his normal activities, if he can walk up a short flight of stairs in relative comfort, and if the contralateral lung field appears normal on roentgenogram, his ventilatory function may be considered adequate to tolerate pneumonectomy. Rarely is it necessary to make specific studies of the oxygen exchange of each lung. Occasionally in the "poor risk" patient with a hilar lesion, angiocardiography may be useful.[9] In this examination failure to opacify the main stem pulmonary artery indicates its occlusion by tumor, thus contraindicating operation because dissection of an adequate length of artery for ligation is improbable.

Although thoracotomy is rarely contraindicated because of poor pulmonary function, lobectomy rather than pneumonectomy for carcinoma may be indicated for a variety of reasons, including borderline ventilatory function, physiologic old age, serious cardiac debility and a combination of physiologic aberrations that combine to form the so-called "poor surgical risk." There is little doubt that a simple lobectomy is less disturbing physiologically and is, in general, better tolerated.

RESULTS

The result of any type of pulmonary surgery depends in large part upon the disease for which it is done. Generally speaking the immediate mortality rate from pneumonectomy is between 5 and 10 per cent and from lobectomy and segmental resection from to 2 to 3 per cent. The number of patients in whom an abscess has been excised has been too small to estimate a true mortality percentage.

In evaluating any particular operation it is wise to divide any series into two groups: those patients operated upon before 1947 and those since that date. In the latter period results have been greatly improved because of a better understanding of the problems encountered in pulmonary resection and the availability of a wide variety of antibiotics.

SUMMARY

Principles of pulmonary resection and their experimental background have been summarized. The management of patients for excisional surgery has been outlined. Improved technic, antibiotics, advances in anesthesia, and a better understanding of pre- and postoperative management have combined to make pulmonary resection the preferential treatment in most pulmonary diseases that require surgical therapy.

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Function Tests in Pulmonary Surgery

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IN selecting the most advantageous operation for pulmonary disease the surgeon is greatly assisted by information from tests of function. In this article we are not concerned with routine function studies, e.g., electrocardiogram and tests of renal and hepatic efficiency, which should be undertaken before all major surgery. We shall discuss only investigations which are of special interest for pulmonary operations.

These tests may be divided into three groups, according to the time at which they are performed: (1) preoperative tests of function; (2) investigations in the immediate postoperative period; and (3) function studies in the later postoperative period.

In the following discussion the groups will be dealt with in turn. For obvious reasons preoperative tests will receive the most detailed consideration.

PREOPERATIVE TESTS OF FUNCTION

Prior to operation the respiratory function may be investigated for motives which to some extent differ: (1) When surgical intervention is strongly indicated these tests enable the case to be classified as functionally operable or inoperable. (2) When pneumonectomy is not unavoidable the function studies are guides in the assessment of the type and extent of operation required. (3) Occasionally defective pulmonary function may in itself constitute an indication for surgery, namely, in conditions in which operative intervention may be expected to improve the function. Such conditions include pulmonary arteriovenous fistula, localized pulmonary emphysema and extensive pleural symphysis.

The complicated nature of pulmonary function has led to the development of innumerable methods for investigating its various important factors. As a result, detailed analyses of function frequently can be performed only in specially equipped physiologic laboratories. From practical considerations, therefore, most surgeons must confine their investigations to a few simple tests. The planning of function tests is thus a current problem.

Since the effect on function is not identical in different pathologic conditions of the lungs, it is essential that, when the results of the tests are evaluated, the diagnosis should be as clear as possible with regard to the etiology and anatomic extent of the disease. Although it may seem superfluous, we must emphatically state that an exhaustive and accurate case history is of fundamental importance for the assessment of a patient's functional capacity. The anamnesis, in addition to relating the course of the pulmonary disease, also provides valuable information of the patient's physical powers. This evidence alone yields a good conception of the cardiopulmonary function. Roentgenographic investigations are, of course, decisive for estimation of the anatomic extent of the disease. It is vitally important that the roentgenographic development of the disease be studied from its start. In pulmonary tuberculosis, for instance, the roentgenograms may show striking clearance of extensive parenchymal involvement, which nevertheless may have given rise to changes deleterious to the later function of the parenchyma. Special attention should also be paid to registration of diaphragmatic mobility, which is of the greatest significance for pulmonary efficiency. Pleural thickening and spinal deformities, as a rule, entail limitation of respiratory function. The same is true of bronchoscopically demonstrable stenosis. Bronchiectatic areas should be carefully mapped out by means of bronchography, which must include the apparently healthy lung. In this connection it should be pointed out that acute bronchitis may give rise to temporary changes in ventilation, gaseous exchange and pulmonary circulation, and so effect a great transitory reduction of respiratory function.

After a thorough standard clinical investigation, most cases of pulmonary disease present

no surgical problem in the estimation of operative possibilities and postoperative effects on function. Because of the great reserves of the human lung, patients with unilateral pulmonary disease and anamnestic evidence of good total function may be submitted to pneumonectomy, partial resection or thoracic collapse procedures without fear of the consequences for respiratory efficiency, provided that future functional demands are not excessive. It is obvious that a lung shown roentgenographically to be destroyed, or a severely diseased lung surrounded by grossly thickened pleura and/or with a poorly mobile diaphragm may for practical purposes be deemed functionless and may be removed without further respiratory investigations. Similarly, it is clear that in severe bronchostenosis the corresponding part of the lung, which invariably shows grave dysfunction, may be resected. The cases which are difficult to evaluate are primarily those with reduced total function and reasonably reliable indications that both lungs contribute to the loss, or which present a combination of pulmonary and cardiac disease. It is in such cases that tests of pulmonary function are valuable complements to the general examination.

In all cases in which surgical therapy is advisable, even in those shown by routine investigations to be clear and uncomplicated, it is nevertheless of interest to check the clinical assessment of total function with a simple and universally applicable test. Determination of the maximal breathing capacity is the simplest method. It provides a measure of the pulmonary ventilation in relation to a time factor. This test has considerable sources of error as its success depends in high degree on the patient's cooperation, the skill of the person conducting the test and the type of apparatus used; but the difference in the ventilation capacity of healthy and diseased lungs generally is so great that the maximal breathing capacity is one of the most reliable indicators of total function. Determination of the vital capacity, on the other hand, which is traditionally used in many clinics as a simple test of function, seems to be less valuable. Although it is not difficult to perform and the results are easily reproducible, the drawback of this test is the difficulty of estimating with a fair degree of certainty the patient's vital capacity under normal conditions. Sometimes the vital capacity may be a misleading indicator of pulmonary efficiency, e.g., in emphysematous persons, who may have a large vital capacity with a low maximal breathing capacity. Of considerably greater interest for pulmonary function in many cases is the residual capacity and its relation to the total capacity, particularly when appreciable emphysema is suspected. A large residual capacity or, more correctly, a residual capacity large in relation to the total capacity, always indicates impaired respiratory function.

As pulmonary surgical procedures with few exceptions reduce function mainly on the treated side, assessment of the efficiency of each lung is of fundamental importance for evaluation of operability in cases of bilateral disease. For this purpose the supreme aid is bronchospirometry, i.e., simultaneous registration of the respiratory function of each lung, by which the oxygen uptake, carbon dioxide elimination, vital capacity and ventilation can be determined. Of these factors the oxygen uptake is decisive as a criterion of pulmonary function. It should be pointed out that in many cases there is considerable discrepancy between ventilation and O_2 uptake, while ventilation and CO_2 elimination are well correlated. By calculating the ventilation equivalent, i.e., the number of liters of air breathed per 100 cc. of O_2 consumption, a good conception is gained of the respiratory efficiency of each lung. When there is doubt of operability, therefore, bronchospirometry is always desirable. In skilled hands it is a fairly simple procedure with a very wide range of indications. Unfortunately bronchospirometry is precluded by some anomalies, such as stenosis of the left main bronchus or marked tracheal deviation, and occasionally is contraindicated in severe bronchitis with copious secretion. If the lung for which surgical treatment is planned is shown by bronchospirometry to possess no more than 10 per cent of the total respiratory function, it may be removed entirely, since to leave one or more segments would contribute nothing to function and would only complicate the operation.

In certain cases in which surgical intervention is clearly necessary, but its extent is in doubt, bronchospirometry performed at the time of operation may give useful guidance. This procedure is recommended primarily for cases in which the requisite topical anesthesia is inadvisable in the preoperative period. Thus

in pulmonary tuberculosis with abundant sputum such anesthesia is considered to carry great risk of spread. The investigation is easily performed with Carlens' double-lumen catheter. This catheter, which was designed for bronchospirometry, has proved to be suitable for the administration of endobronchial anesthesia in pulmonary operations. As each lung is ventilated separately, "spill over" is prevented and the operation is facilitated by the fact that either lung can be separately collapsed. Immediately before the general anesthesia is induced the tubes of Carlens' catheter can be connected to a double spirometer or, if this is not available, to two instruments for recording basal metabolism, and bronchospirometric tracings made. The results may be decisive for the form of operation.

Bronchospirometry, however, has the disadvantage that the patient is studied while he breathes with both lungs and without a reduction of parenchyma corresponding to that proposed by the operation. In borderline cases, therefore, it is not always possible to determine by bronchospirometry how the pulmonary function will be affected after surgery, or if the patient will tolerate being temporarily deprived of some pulmonary parenchyma during the operation. In such cases, and when bronchospirometry cannot be performed or is contraindicated, information of the individual function and operability of the lungs may be gained from occlusion of the pulmonary artery, or one of its larger branches, to the lung for which operation is planned. Using a modified heart catheterization technic, occlusion is achieved by means of an inflatable rubber cuff mounted on the catheter. The pulmonary arterial circulation is thus completely cut off in the occluded area and estimation may be made of the effect on oxygen uptake and pulmonary circulation of a reduction of the vascular bed corresponding to the extent of the contemplated resection. The technic of pulmonary artery occlusion, therefore, has provided a means whereby the patient's postoperative capacity can be predicted prior to the intervention. If moderate exercise is performed while the pulmonary artery is occluded, the picture is complete.

Because of the close integration of cardiac and pulmonary function, heart catheterization and pressure measurements in the pulmonary circulation, with and without occlusion of the pulmonary artery, are also indicated when there is reason to suspect pulmonary hypertension or cardiac disease. In our experience, verifiable pulmonary hypertension is seldom present during rest, even in patients with fairly extensive bilateral lesions. As a rule, however, only very light exercise is required to produce pressure increase in these patients. In the relatively few patients in whom the resting pulmonary arterial pressure is definitely raised the long-term prognosis is poor.

In addition to the foregoing methods of studying the total and individual pulmonary function, useful information may be gained in the more complicated cases from measurement of the arterial oxygen saturation or, preferably, the arterial oxygen tension under conditions of rest and exercise, and also with the pulmonary artery occluded. Even in many cases of pulmonary tuberculosis with old, extensive lesions the O_2 tension and saturation are not notably decreased during rest. On the other hand, patients with severe fibrotic lesions which have given rise to considerable emphysema or are complicated by pneumoconiosis frequently show appreciably diminished arterial oxygenation both at rest and during exercise. This constitutes an indicator of great practical importance for surgical evaluation. Blood gas analysis is particularly important in arteriovenous aneurysm of the lung and in localized emphysema, in which conditions there is a considerable shunt.

The interpretation of lung function tests and the resultant assessment of surgical possibilities must be carefully correlated to the etiology and general prognosis of the basic disease. Modern technics in pulmonary surgery and improved methods of anesthesia have made it possible to operate, with very low mortality, upon patients with bilateral lesions and greatly reduced respiratory function. Even when operation has to be performed on the lung with the better function, the most critical period—during and immediately after the operation—is often surprisingly well tolerated. The risk in pulmonary surgery is thus in many cases not so much the direct operative mortality as the making of respiratory cripples.

In cases of pulmonary cancer in which surgery is the only means of saving life, relatively large risks are justifiable as regards both immediate mortality and cardiorespiratory invalidism. Such patients are generally in the higher age groups and therefore emphysema

must be reckoned with, possibly co-existing with old tuberculous changes or cardiosclerosis.

In operations for bronchiectasis the determining factor is the anatomic extent of the disease. As a rule the indications for surgery are not so urgent in bronchiectasis as in other conditions, especially cancer. If pulmonary function studies make operability doubtful, one may advise against surgery and instead recommend conservative therapy.

The greatest difficulties in evaluating respiratory efficiency are encountered in many patients with pulmonary tuberculosis. In such patients it is of paramount importance that the tests be carried out when the general condition has been improved as far as possible by sanatorium care. And as frequently a choice must be made between several surgical procedures, investigations of pulmonary function must be thoroughly carried out and adapted to meet the individual features of each case. In evaluating surgical possibilities in pulmonary tuberculosis it must not be forgotten that operation sometimes improves respiratory function. Pleural empyema or bronchopleural fistula with secondary bronchitis and copious sputum may, as previously mentioned, have a highly unfavorable effect on pulmonary efficiency. A resection procedure with removal of the empyema sac or fistula will abolish the bronchial irritation and considerably improve lung function. Removal of a thickened pleura and correction of a mediastinal shift will also have a very favorable effect in some cases.

INVESTIGATIONS IN THE IMMEDIATE POSTOPERATIVE PERIOD

In patients with severely reduced pulmonary function close study of the O_2 and CO_2 content of the arterial blood is vitally important in the immediate postoperative period. Early detection of CO_2 retention is particularly essential. Every major thoracic intervention is followed by a considerable lowering of the arterial O_2 tension and saturation, which usually persists for three to six days. The arterial CO_2, however, is only insignificantly increased in this period. But ventilatory insufficiency will very rapidly bring about CO_2 retention. To counteract this, ventilation must be intensified and the bronchi kept as clear as possible by aspiration. If, despite such measures, the CO_2 retention increases, tracheotomy should be performed without delay. In this way the "dead space" is diminished by about 100 cc., alveolar ventilation is improved and bronchial cleansing facilitated.

FUNCTION STUDIES IN THE LATER POSTOPERATIVE PERIOD

When pulmonary function has become stabilized after the operation, its assessment may be of interest from several aspects. It may be necessary, for instance, to estimate working capacity and possible disability for insurance and pension purposes. In the preoperative investigations the patient as a rule cooperates wholeheartedly and gives accurate information concerning respiratory and general physical capacity. But in evaluation mainly for economic purposes the patient will often present an exaggerated account of his discomforts. Objective tests of pulmonary function are therefore necessary. The methods primarily to be employed are determination of the maximal breathing capacity and graded exercise tests of total physical capacity. Then come estimation of the residual capacity, bronchospirometry and blood gas analysis.

Finally, the value of postoperative studies purely for research purposes should be stressed. From sufficiently large series of typical interventions it should be possible to draw valuable conclusions concerning the functional significance of various parts of the parenchyma. These circumstances are as yet very imperfectly understood, but may prove to be of great importance for the choice of surgical procedure in individual cases.

SUMMARY

In the preoperative evaluation of pulmonary function the results of clinical investigations are decisive for the question of operability and for the choice of intervention. Great importance is attached to the anamnesis. All available roentgenograms must be carefully studied, the anatomic extent of the disease noted and diaphragmatic and costal mobility assessed. Inspection of the bronchial tree is also important. In some cases bronchography is advisable.

A simple and practical test of pulmonary function is registration of the maximal breathing capacity. In more doubtful cases spirometry with determination of the residual capacity is advised.

For estimation of the individual pulmonary

function, which is of great practical importance when planning surgery, bronchospirometry is the most valuable aid and may be used on very wide indications. There are few contraindications to its use and in the great majority of patients it is easily performed. When bronchospirometry is not possible or is contraindicated, heart catheterization with occlusion of the pulmonary artery may be carried out. This applies chiefly to patients in whom tests of total function and bronchospirometric findings leave doubt of operability.

Heart catheterization, with or without occlusion of the pulmonary artery, and possibly during exercise, may also be contemplated when greatly impaired total function or clinical evidence of cardiac disease indicate pulmonary hypertension. Severe hypertension carries an unfavorable prognosis.

Blood gas analysis of samples taken at rest and during exercise, and also with the pulmonary artery occluded, may provide valuable complementary information in patients with severe pulmonary emphysema or other changes which impair the gaseous exchange in the lungs.

In the immediate postoperative period continuous study of the blood gases is extremely important for the early detection of CO_2 retention.

Postoperative studies of pulmonary function are useful particularly for estimating working capacity or disability for such purposes as insurance. By appraisal of the respiratory efficiency some time after the operation valuable knowledge may be gained of the effects of various surgical procedures on respiratory function.

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Anesthesiology in Pulmonary Surgery: Special Problems

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ONE of the major problems in pulmonary surgery is the organization of a surgical team. Because of its complexity, modern surgery has become a group enterprise and is most successfully carried out by a team of cooperating specialists. Pulmonary surgery with its extra complexity requires even more exactly the coordinated efforts of a surgical team. The details that must be constantly attended to are so numerous that one physician cannot possibly handle them as well as can a team of physicians and assistants. To be effective teamwork implies, first, a willingness to cooperate and, second, practice in coordination of individual efforts. The establishment of a smoothly functioning surgical team is a problem and a responsibility of both the surgeon and the anesthesiologist.

The thoracic surgeon's problems must be understood and appreciated by the anesthesiologist. One of the special problems of the anesthesiologist is to avoid becoming so engrossed in his own difficulties that he fails to appreciate the objectives of the surgical team as a whole. Simple as it may seem to others, it is not always easy for the anesthesiologist to remember that few patients come to the hospital for the purpose of receiving anesthetics and to admit that anesthesia is only a means by which an end is obtained.

On the other hand, the problems of the anesthesiologist are also the problems of the surgeon and the other members of the surgical team. When the anesthesiologist is in trouble, the welfare of the patient may be threatened; and it behooves the others on the team to lend as much cooperation as possible until the danger has passed. This give or take in the proper direction and in the correct degree requires a common understanding of the personalities of all members of the team and an unselfish desire on the part of all to promote the welfare of the patient. The decision as to what is best for the patient should be the rule by which all misunderstandings among the members of the team are settled.

The problems of the anesthesiologist in pulmonary surgery are those of general surgery plus the special problems imposed by the fact that the site of operation is the organs of respiration. For most surgical procedures it is considered imperative for the parts being operated upon to be immobilized and at rest during the operation. It would be impossible for an orthopedist to operate on the leg of a patient who is walking or for an ophthalmologist to operate on the eye of a patient who is reading a newspaper. Yet the thoracic surgeon is forced to operate on the respiratory organs while they continue to carry on their function. To date, no practical method has been developed to oxygenate the blood artificially so that the lungs and other parts of the respiratory mechanism may be inactivated.

After the control of sepsis allowed rapid advances to be made in most fields of surgery, technically competent surgeons with adequate knowledge of intrathoracic anatomy were available for progress in pulmonary surgery; but these surgeons soon learned from experience that patients with the thorax open did not survive long enough for detailed operations to be performed. Therefore progress in pulmonary surgery had to wait for the development of anesthesiology and methods for artificially maintaining adequate respiratory exchange during intrathoracic operations. The specialty of anesthesiology should not be overly proud of its accomplishments in solving this problem. There are still many unanswered questions, and even the simple basic principles have been learned and applied very slowly. It is still advantageous to review some of the alterations in physiology caused by opening the thorax, and some of the technics whereby these alterations may be corrected. Most of the special

problems in anesthesiology as related to pulmonary surgery are concerned with the maintenance of adequate respiration and adequate circulation.

MAINTENANCE OF ADEQUATE RESPIRATION

Pneumothorax. The thorax may be compared to a semi-rigid cylinder and the diaphragm compared to a piston. As the diaphragm descends, negative pressure produced in the thorax causes air at atmospheric pressure to flow down the tortuous air passages to enter the alveoli and fill the lung to the extent that the negative pressure in the thorax is almost neutralized. If the thoracic wall has an opening which offers less resistance to the passage of air or gas than do the tortuous normal air passages, much air will enter the pleural space to neutralize the negative pressure caused by contraction and descent of the diaphragm, and the volume of gas entering the alveoli is thereby decreased. The solution of this problem is to deliver the respiratory gases to the patent airway at a pressure greater than atmospheric pressure. This pressure at the airway must be sufficient to overcome the difference between the resistance through the pulmonary air passages and the resistance through the opening in the pleura and still remain greater than atmospheric pressure. The application of such a pressure facilitates the passage of gases into the alveoli but retards the removal of gases from the lung. If positive pressure helps inspiration and hinders expiration, it is logical that the pressure should be applied intermittently, that is, during inspiration only.

Two methods of artificial respiration are favored at the present time in this country: assisted and controlled respiration. By the assisted technic the respiratory center and muscles are allowed to remain active. The application of pressure to the respiratory gases is synchronized to coincide exactly with inspiration and then the pressure is released to allow passive expiration. By the controlled technic either the respiratory center or the respiratory muscles or both are rendered inactive and the positive pressure necessary to inflate the lungs adequately is applied intermittently at a rate and rhythm determined by the anesthesiologist. When properly used, either of these technics can provide adequate and safe operating conditions, as evidenced by their widespread use. Most anesthesiologists have their preference for one or the other of these technics. We prefer the assisted technic because it has given us good results and seems to maintain more constantly the homeostasis of the patient, particularly as concerns the acid-base balance.

When gas mixtures with high oxygen tension are being respired, the blood may be kept oxygenated by an exchange of gases that does not adequately eliminate the carbon dioxide from the blood, as shown by Beecher. Under these conditions a greater minute volume of respiration is necessary for the removal of enough carbon dioxide from the blood than is required for the addition of enough oxygen to it. In the normal unanesthetized person the carbon dioxide content of the blood is maintained within almost unbelievably narrow limits in order to keep the pH of the blood within still narrower limits. Even minor changes in blood pH are poorly tolerated and hence slight changes in carbon dioxide tension in the normal person are immediately followed by subjective symptoms and compensatory changes in the respiratory pattern. These protective respiratory reflexes are activated through the respiratory center and cannot be utilized if either the respiratory center has been paralyzed with depressant drugs or the respiratory muscles have been paralyzed with curare. Until such time as instruments are available for continuous monitoring of the pH of the blood, we believe that our patients are safer when the respiratory center is kept active to direct our otherwise blind efforts to maintain homeostasis of the acid-base balance.

While the pH of the blood must be kept within narrow limits if the patient is to survive, some accommodation to minor increase or decrease in pH is possible. Concerning the acidosis accompanying cyclopropane anesthesia, Dripps has expressed the belief that it is the rapidity of change in the pH of the blood that is most important. With assisted respiration and an active respiratory center the anesthesiologist is compelled to maintain the minute volume of respiration and hence the blood pH at a more constant level. With controlled respiration there is a tendency to hyperventilate the lungs prior to a period when the anesthesiologist plans to stop artificial respiration for a short time in order to perform some other duty. Such marked variations in pulmonary venti-

lation must result in rapid changes in blood pH if the periods of hyperventilation and hypoventilation are of appreciable duration.

This problem of maintaining a constant ventilation rate brings up the question as to whether or not machines should be used to perform artificial respiration in patients undergoing pulmonary operations. Such a practice has been commonly used for anesthetized animals in the laboratory for many years and has seemed to serve a useful purpose when trained anesthesiologists were not available. The use of machines for respiration has been in much greater favor in Europe than in the United States. Mushin and Rendell-Baker have reviewed the various types of apparatus which have been recommended for artificial respiration in man. Not one of the machines has been considered satisfactory by a large percentage of thoracic surgeons or anesthesiologists. We have not had the privilege of trying all of the apparatus which have been advocated, but in the experience we have had we have not been pleased with the performance of any type in all operations. Since the demand for a simple and efficient apparatus for maintaining pulmonary ventilation at the indicated rate will increase as the volume of intrathoracic surgery increases, the market may soon stimulate the interest of those persons capable of developing such a machine.

Occasionally both pleural spaces may be opened and bilateral pneumothorax produced. This is most likely to occur during operations which involve the posterior or anterior mediastinum. When the surgeon realizes that both pleural cavities have been opened, he should notify the anesthesiologist at once since the latter may have no other means of knowing that the complication has occurred. This is true even if the hole in one pleura is very small, because greater diligence will be needed to prevent collapse of both lungs, and the preparation of additional equipment may be indicated as a precautionary measure. The possibility that tension pneumothorax may occur on the side opposite to the one on which the thorax was entered must be kept in mind. The occurrence of bilateral pneumothorax need not be particularly alarming provided all the team knows about it. Frequently the lung opposite the side being operated upon may be inflated by applying extra pressure in the pulmonary system and then closing the hole in the pleura on that side with a suture or a covering pack. If indicated, the hole may be left open until the intrathoracic part of the operation is completed provided adequate artificial respiration is assured. Before the thorax is closed, all air should be removed from both pleural spaces and some means established to make certain that any air which subsequently enters either side will be promptly removed.

As has been intimated, the use of constant positive pressure is not as efficacious in promoting adequate pulmonary ventilation in the patient with an open thorax as either assisted or controlled respiration. Constant positive intrabronchial pressure up to 10 mm. of mercury for short periods may be useful for inflating the lungs. This may be particularly helpful during segmental resection of a lobe or at any time that the distribution of a particular bronchus must be known.

On rare occasions it may be necessary to increase the intrabronchial pressure to 15 mm. of mercury above atmospheric pressure to produce the desired inflation of a lung, but this pressure should be maintained for only very brief periods. Contrary to the advice of many anesthesiologists, we have not found it necessary routinely to inflate at regular intervals during the operation the lung on the side being operated upon. Even when a lung has been kept completely collapsed for several hours, we have not had any difficulty in reinflating it with intermittent applications of 10 to 15 mm. of positive pressure. Of course if the bronchus is occluded, no reasonable intrabronchial pressure will inflate the lung. A lung which has been collapsed for weeks or months by some process such as empyema or pressure by a tumor will inflate more slowly than a lung which has been functioning up until the time the thorax is opened. Attempts during operation to inflate such chronically collapsed lungs completely should not be too vigorous. It is better to complete the inflation by the maintenance of negative intrapleural pressure during the immediate postoperative period.

Sometimes inflation of a previously deflated lung results in patchy atelectasis. It is simpler and safer for the surgeon to massage these atelectatic areas while mild intrabronchial pressure is being maintained than it is to rely entirely on dangerously high pressures alone to produce the uniform inflation desired. Both the surgeon and the anesthesiologist should

be responsible for making sure that every segment of the lung is inflated before the thorax is closed. The time when the thorax is open and the lung is in the hand of the surgeon is the most favorable one for securing complete inflation. With the patient in the lateral position the anesthesiologist is sometimes in a more favorable place than the surgeon to observe the lower lobe of the lung and to notice small uninflated areas.

Mediastinal Shift. When a normal person with a movable mediastinum lies in a lateral position, the weight of the heart causes the mediastinum to be moved toward the downside and thereby to compress the lower lung. (Fig. 1.) Cardiac hypertrophy, intrapleural fluid or a large heavy mass in the upper lung exaggerates this problem. Then when pneumothorax is produced in the upper pleural cavity, the neutralization of the negative pressure in that cavity allows still further displacement of the mediastinum onto the lower lung. Even more important is the tendency for the mediastinum to move toward the compressed lower lung during inspiration when the negative pressure in the lower pleural cavity is increased by descent of the diaphragm. In turn, during expiration, the mediastinum is forced back to the position it occupied before inspiration. The ventilation of the lower lung is thus decreased by the volume of the space through which the mediastinum moves with each respiratory cycle. In our opinion this so-called mediastinal flutter is detrimental primarily because of its inhibition of respiratory exchange and not so much because of any circulatory reflexes which it initiates. It is true that circulatory symptoms do eventually occur, but we believe that they are most frequently secondary to inadequate respiration.

If in addition to the downward displacement of the mediastinum onto the only intact lung a rest or support is placed under the thorax, the lower thoracic wall is pushed up so that it almost meets the inferior portion of the mediastinum in which the heart is located. (Fig. 1.)

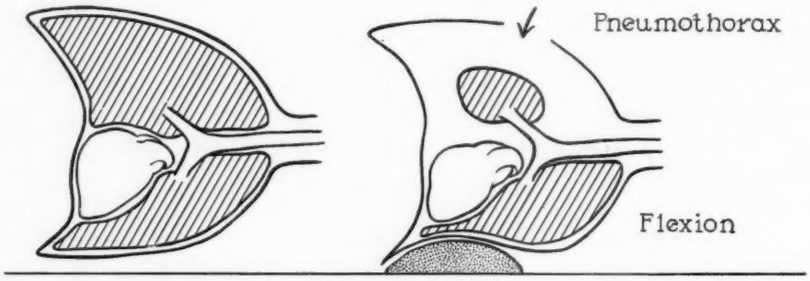

FIG. 1. Reduction in functioning pulmonary volume resulting from pneumothorax in the upper pleural cavity of a patient in the lateral position with an elevation under the thorax.

Now with the upper lung collapsed by pneumothorax and the inferior lobe of the lower lung pinched between the mediastinum and the rest or support on the table, the only functioning pulmonary tissue left is the superior lobe or lobes of the lower lung. For this reason we believe that no elevating mechanism should be used under the thorax of the patient who is lying in the lateral position during a pulmonary operation.

These problems, which are peculiar to the lateral position, are known to all thoracic surgeons, but their extent and their seriousness are not always appreciated. In either lateral position the upper (lateral) border of the heart is usually even with or below the bodies of the thoracic vertebrae, which means that the volume of the intact lower lung is reduced an amount equal to the volume of the heart. The advantages and disadvantages of the prone position as compared to the lateral position will not be discussed here since they are presented in another article in this issue.

Paradoxic Respiration. Regardless of whether an operation on the lung is performed with the patient in the lateral, prone or supine position, paradoxic respiration is a problem. (Fig. 2.) Such respiration is a paradox in that the lung in the open side of the thorax tends to collapse during inspiration and expand during expiration, which is just the opposite of the lung on the intact side. Thereby, during the respiratory cycle, gases are shuttled back and forth from one lung to the other without

supplying oxygen or eliminating carbon dioxide. This severely decreases effective respiration and when marked cannot be tolerated for long.

Paradoxic respiration may be eliminated by preventing the lung on the side of the pneumothorax from changing in volume. If the lung on the side being operated upon does not have to be used in order to provide adequate respiration, it may be maintained in a completely collapsed position by covering it with heavy gauze dampened with physiologic salt solution. Such a maneuver greatly facilitates the surgeon's exposure and promotes progress of the operation. The high intermittent endobronchial pressure of the respiratory gases frequently necessary to insure adequate respiration by the technic of controlled artificial respiration and occasionally necessary with the assisted technic tends to inflate the lung on the operated side, but such must be tolerated if the safety of the patient would otherwise be jeopardized. The goal in assisted respiration is to apply the positive pressure at just the right time in the right amount to keep the lung on the operated side at exactly the same volume and the mediastinum at exactly the same position at all times. This goal is almost impossible to attain but should be approached as closely as the skill of the anesthesiologist will allow. In this way only can detrimental paradoxic respiration be prevented when the assisted technic of artificial respiration is being used. Since no respiratory efforts are allowed to occur when controlled respiration is used, paradoxic respiration is not a problem.

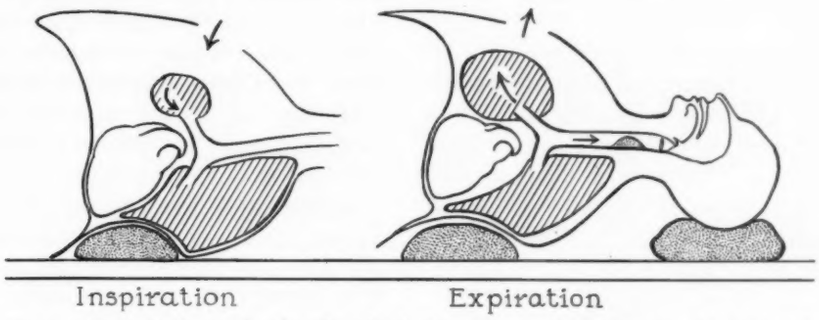

FIG. 2. Paradoxic respiration in which the volume of the lung on the side of the open pleura decreases on inspiration and increases on expiration.

Respiratory Obstruction. One of the vital requirements for the promotion of adequate respiration is the maintenance of freely patent connections between the alveoli and the atmosphere for the passage of gases between the two. The normal passages are crooked and small so that some resistance to the flow of gases exists. Any decrease in the cross section of the air passages causes a pronounced increase in the resistance to gas flow and hence greatly increases the effort necessary for an adequate respiratory exchange. If the detriments to respiration already outlined are allowed to continue uncorrected and the maximal effort is being exerted to effect adequate pulmonary ventilation, even partial obstruction of the airway may result in death of the patient. When the respiratory mechanism is crippled by a combination of the factors named, greater respiratory effort may compensate for the inefficiency of the mechanism for a short time. However, respiratory muscles are not adapted to heavy work and they soon tire, so that if the unfavorable conditions persist for many hours, the respiratory compensation may gradually fail, unrecognized chronic anoxia ensue and unexpected sudden death occur. Such an unrecognized complication might well be diagnosed cardiac arrest of undetermined cause or perhaps considered the result of a vagovagal reflex.

The use of a satisfactory intratracheal tube reduces the likelihood of obstruction in the upper respiratory passages and has come to be regarded almost as a necessity in pulmonary surgery. The anesthesiologist must not, however, put implicit faith in such a tube and must be constantly aware of the possibility of the failure of the tube to assure an unobstructed airway. Such a failure may occur because of compression of the tube by the patient's teeth, kinking of the tube, approximation of the intratracheal end of the tube against the wall of the trachea or other unusual complications.

Obstruction of the lower air passages by

mucus, secretions, blood, bits of tumor and foreign bodies is more difficult to prevent and to relieve. The experience of the anesthesiologist, his knowledge of pulmonary pathology and his familiarity with the individual technics of the surgeon are invaluable in selecting patients with whom special precautions should be taken.

So-called wet lung patients are operated upon much less frequently now than fifteen years ago, before antibiotics became available. Preoperative preparation of bronchiectatic patients with aerosol and parenteral administration of indicated antibiotics has almost eliminated the greatest source of patients with profuse bronchial secretions who are presented for anesthesia and operation at our institution. Such treatment greatly reduces the volume of the bronchiectatic secretions, but also makes them more tenacious and more difficult to remove with an aspirating catheter. Chronic pulmonary abscess and empyema associated with bronchopleural fistula are the source of most of the profuse bronchial secretions we encounter today. Endobronchial tubes are generally used in operations upon patients with profuse bronchial secretions in order to prevent the secretions from entering and occluding the bronchi of the uninvolved lung.

Bleeding into the tracheobronchial tree is particularly dangerous during pulmonary operations. Secretions remain fluid and continue to be moved back and forth during respiration so that they can be removed from the sites which can be reached with an aspirating catheter. Blood enters the bronchi as a liquid but turns to a gel or solid in the smaller bronchi from which it cannot be aspirated blindly and cannot be expelled by respirations or mild cough. Some of our most harrowing experiences have been with bleeding into the bronchi. Such bleeding is more likely to be encountered during operations upon patients with bronchial adenoma, bronchial carcinoma or bronchiectasis. An open bronchus in a bloody field is always a source of danger and should be avoided. Fortunate is the anesthesiologist who works on a pulmonary surgical team with a surgeon who in the face of such emergencies is able to disregard routine surgical procedures and can quickly clamp the bronchus through which the blood is entering the tracheobronchial tree. Once the source is stopped, the anesthesiologist has a fighting chance to remove the blood in the bronchi before it coagulates.

Removal of blood and secretions from the bronchi is more readily accomplished when the patient is lying on his right side than when he is lying on his left side. This is due to the fact that the blood and secretions flow toward the lower side, and the right main bronchus is more easily entered with a catheter than is the left main bronchus. Catheters with a curved tip such as the Coudé and Bardam catheters facilitate blind aspiration of material from the left bronchi. The addition of extra small holes near the tip of the catheter decreases the time needed for aspiration.[5] The danger of prolonged aspiration is not widely appreciated. Burchell has shown that pronounced decreases in arterial oxygen saturation may occur during the time that secretions are being aspirated from the lower respiratory air passages. This maneuver should be used only when necessary and for as short a time as possible.

Blood clots and solid particles are not easily removed blindly with a flexible aspirating catheter introduced through the intratracheal tube. Usually bronchoscopy is necessary for the removal of foreign bodies of this nature. All anesthesiologists on thoracic surgical teams should be familiar with the technic of bronchoscopy, and such an instrument should be available on short notice since the patient's life may depend on the rapidity with which the instrument is efficiently used. Whether or not it should be a routine practice to perform bronchoscopy after thoracic operations is still debatable. Although we have had the privilege of participating in routine postoperative bronchoscopy on certain surgical services while at the same time the procedure was not being done on other surgical services, we still have not formed a definite opinion for or against it. There is no doubt that it carries some risk, and rarely a patient has died during the procedure. On the other hand, its routine use has uncovered many unsuspected abnormalities. An example is a ten year old child from whose left lower bronchus a head of grass seed was removed during routine postoperative bronchoscopy following a right lower lobectomy for pulmonary abscess. During the manipulation at operation the seed head, which had apparently caused the abscess in the right lower lobe, was dislodged and fell into the left

bronchus. It would undoubtedly have caused another abscess there if bronchoscopy had not been a routine practice.

If postoperative bronchoscopy is not to be done, the respiratory passages should be thoroughly cleared of all secretions before the patient leaves the operating room and before the intratracheal tube is removed. The secretions which frequently accumulate in the nasopharynx should be removed in order to save the patient from having to cough them out later when his thorax is painful.

MAINTENANCE OF ADEQUATE CIRCULATION

The special problems in the maintenance of adequate circulation during pulmonary operations may be placed in two categories: reflex and mechanical.

The periosteum of the ribs, the pleura and the larger bronchi are sensitive tissues, and trauma to them during operation may result in adverse circulatory changes through reflex mechanisms. Afferent impulses from these thoracic tissues may initiate a discharge of efferent impulses over the vagus nerves to cause bradycardia, decrease in cardiac output and fall in blood pressure. This is sometimes called a vagovagal reflex since both afferent and efferent impulses are thought to be conducted over vagal nerve fibers. Such a reflex has been thought to be a common cause of cardiac arrest, but we have not encountered a case in which we could be sure that such was the sequence of events. From clinical reports there apparently is considerable difference in the depressing effects of various anesthetic agents on these circulatory reflexes. Since we have been using ethyl ether as the primary anesthetic agent for most intrathoracic operations, we have had very few adverse circulatory reflexes result from hilar dissection, clamping of a bronchus or ligation of a pulmonary vessel. Infiltration of the hilus with procaine or intravenous administration of atropine has not been found necessary in our practice. Rarely the intravenous use of procaine has been helpful in abolishing persistent premature ventricular contractions, but not any more frequently during intrathoracic than during intra-abdominal surgical procedures.

Perhaps the fall of blood pressure which occurs immediately after the change of the patient's position on the operating table at the end of a long operation should be classified as a reflex change. It is likely due to the fact that anesthesia inhibits the circulatory reflexes which normally accommodate to changes in position. However, fall in blood pressure consequent to change from the lateral to the supine position seems to be more frequent and more severe following intrathoracic operations than following operations at other sites. Such changes in blood pressure can be minimized by gentle handling of the patient and slow change in the position. If a fall in blood pressure does occur, it can frequently be corrected by elevation of the patient's legs for a few minutes after he is in the supine position. If this does not produce the desired rise in pressure, blood transfusion should be considered. Tension pneumothorax may be the cause of a fall in blood pressure when the patient is turned from the lateral to the supine position, owing to a return of the mediastinum toward the upper or operated side.

The mechanical effects on circulation are more definite. Care must be exercised to allow no pressure on the heart and not to retract it very far from its normal position in attempting to secure exposure in the thorax. Such a mistake is more likely to be made during intrathoracic procedures on infants in whom more than the slightest retraction may be excessive. The adverse effect is probably due both to compression of the heart itself and to partial kinking of some of the great vessels near the heart. No openings should be left in the pericardium through which the heart might be able to herniate to an abnormal and less efficient position.

The loss of the sucking effect of normal negative pressure in the thorax and the production of an increase in intrathoracic pressure by artificial respiration or tension pneumothorax tend to decrease the return of venous blood to the heart. Unless other mechanisms compensate for the decrease in venous return, cardiac output and blood pressure will decrease. Machines for artificial respiration which produce alternating positive and negative pressure have been advocated to prevent these adverse circulatory effects of positive pressure. In clinical practice the intermittent use of moderate degrees of positive pressure for periods of time equal to normal inspiration has not seemed to be detrimental to efficient circulation.

The large caliber, short length and thin walls

of the pulmonary blood vessels make severe hemorrhage a constant threat during pulmonary operations. Because of the necessity for ligation of the vessels close to the pericardium and heart, hemorrhage is not as easily controlled here as in other parts of the body. Hence preparation for adequate replacement of blood should be made before the surgical drapes are put in place. It is our practice to insert a 15 gauge needle in the internal saphenous vein at the ankle. When the patient is to be in the lateral position, the lowermost leg is used. Another 15 gauge needle either is inserted in a vein in a hand or forearm or is prepared for insertion so that it will be available should an emergency arise that would demand rapid administration of blood. The Edison airway-needle clamp* has been found practical for the administration of blood under pressure, but its use demands the constant attention of a responsible person to prevent intravenous insufflation of air. When the left side of the thorax is operated upon, the proximity of the aorta makes intra-arterial transfusion relatively easy with a minimum of apparatus and loss of time; but this procedure has rarely been found necessary. Caution must be exercised during the excitement of rapid hemorrhage that the loss of blood is not overestimated; otherwise excessive transfusion of blood may result in pulmonary edema. Pulmonary edema would seem to be more easily precipitated when only one lung is functioning after pneumonectomy than when both lungs are functioning.

EQUIPMENT

We intentionally have not mentioned the selection of anesthetic agent, method or special technic. Many agents and combinations of agents have been used to produce consistently results that are satisfactory to surgeon, patient and anesthesiologist. This record is evidence that no one agent or combination is the ideal to the exclusion of all others. If the anesthesiologist understands the special physiologic and anatomic problems involved in pulmonary surgery and is familiar with all the pharmacologic actions of several anesthetic and related drugs, he can easily select the pharmacologic agents he needs to solve his problems.

Anesthesia equipment should be kept simple in order to insure its efficiency. The criticism too often justly made of anesthesiologists responsible for anesthesia in pulmonary surgery is that frequently their equipment fails to work. When a needle gets out of the vein, an endotracheal tube cuff leaks, an aspirating catheter is not satisfactory or an artificial-respiration machine fails to function adequately, the results are likely to be inconvenient to the surgeon and they may be disastrous to the patient. These accidents seem to occur most often at a critical stage of the operation. The attention devoted to the adjusting of complicated equipment must of necessity be subtracted from the attention and time which the anesthesiologist should be devoting to the observation and care of his patient. Precautions should be taken to see that all equipment is in good working order before anesthesia is begun. If the anesthesiologist is not able or willing to devote the time necessary for the preparation of efficient equipment, he must take a lesson from the surgeon and arrange for responsible persons to perform this necessary task for him. When the patient's thorax is open and he is vitally dependent on the anesthesiologist for the maintenance of adequate pulmonary ventilation, it is no time for makeshift repair of equipment.

* Thomas A. Edison, Inc., West Orange, N. J.

SUMMARY

Among the special problems that confront the anesthesiologist in operations on the lungs are those related to (1) the maintenance of adequate respiration, (2) the maintenance of adequate circulation and (3) the selection of simple but efficient anesthesia equipment.

The maintenance of adequate respiration necessitates the handling of such problems as those presented by pneumothorax, mediastinal shift, paradoxic respiration and respiratory obstruction.

The maintenance of adequate circulation necessitates the handling of reflex and mechanical problems. The reflex phenomena, such as bradycardia, decrease in cardiac output and fall in blood pressure, are often thought to be related to the so-called vagovagal reflex. The mechanical problems are brought about by such factors as pressure or traction on the heart or great vessels, changes in the pressure relationships between the intrapleural and the intrapulmonary spaces, and hemorrhage.

Anesthesia equipment should be kept simple in order that its efficiency may be assured.

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Operative Positions and Approaches in Pulmonary Surgery

VALUE OF THE SUSPENDED PRONE POSITION

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THE selection of position and approach for thoracic surgical procedures may constitute an important consideration since these procedures, particularly pulmonary resection, frequently present the problems of the control of secretions and the maintenance of adequate ventilatory function. A correct position minimizes disturbances in the cardiorespiratory physiology of the patient and an accurate approach provides for an optimum exposure for the surgeon. In general, the positions used for pulmonary excisional surgery are the lateral, supine and prone; of these the one most frequently employed is the lateral. The selection of the position is dependent upon the nature and location of the disease process. Surgeons, however, have a tendency to use the position they are most accustomed to, which in some instances may create difficulties for the surgeon as well as the anesthetist and may result in complications in the patient.

During the past decade experience with the use of the various positions in the surgical treatment of patients with considerable intrabronchial suppuration, e.g., lung abscess, bronchiectasis, malignancy with abscess formation, tuberculosis with suppuration, and associated bronchopleural fistula and empyema has led the author to select the prone position as the one of choice in the performance of pulmonary resection.[1]

The purposes of this paper are (1) to discuss briefly the operative positions and approaches in pulmonary resection, (2) to enumerate the advantages and disadvantages of the lateral position as contrasted to the advantages and disadvantages of the prone, (3) to present certain aspects of a specially designed apparatus for face-down surgery and (4) to point out that the complications reported with the use of the prone position are the result of its improper use. In addition, suggestions will be made for the prevention of shock in the poor risk patient.

Anterior Approach: Supine Position. In general the two routes of access to the pleural cavity in frequent use are the anterior and posterolateral approaches. With the anterior approach the patient lies supine on the table with a small pillow or sandbag under the shoulder of the affected side to permit extension of the incision farther into the axilla, if desired. The pleural cavity is entered by an intercostal incision in the fourth interspace or removal of the fourth rib, extending from the mid-axillary line to the sternum. Increased exposure is obtained by dividing the cartilage parasternally above and below the line of the incision.

The anterior approach is excellent as far as the physiologic structure and function of the patient's thorax are concerned; the lung on the unaffected side is able to function without embarrassment. It has the further advantage of reducing the time required to open and to close the chest, a consideration of importance in prolonged cases.

The disadvantages of the anterior approach are several. (1) If the lung is firmly fixed to the chest wall, the technical difficulties to freeing it become insurmountable and much of the dissection has to be done blindly, particularly at the posterior apex and in the costophrenic angle. (2) If the lung is edematous and non-collapsible, there may not be enough working space to deal with peripheral attachments and with the hilar dissection because of the limited thoracic cage spread. (3) A lower lobectomy is more difficult through the anterior approach than it is when performed posteriorly. (4) If the ribs or cartilages have been divided, as they almost always are, the chest wall is somewhat less stable than after the posterior incision when the scapula and attached muscles lend stability to the operative

site. (5) There is a risk of infection of the cartilages if the wound becomes infected; in instances in which the sternum is cut the chances of it becoming infected is even greater. (6) Lastly, in diseases with marked pulmonary secretions bronchial drainage is impeded because the trachea in its cephalad course assumes a more ventral position. To overcome this point anesthetists usually place the patient in a moderate Trendelenburg position; but in so doing, the abdominal contents are forced to gravitate against the diaphragm due to the rigid spine posteriorly and the rigid lower ribs on either side, thus diminishing respiratory exchange.

Chamberlain[2] in the following article appearing in this symposium, maintains that "the anterolateral incision for pulmonary operations is to be condemned since only the most skillful surgeon can afford such a handicap." According to him the anterior approach was popular in the early development of thoracic surgery because it was fast and there was less mediastinal flutter. He also points out that "the surgeon who has encountered hemorrhage in an open chest can alone appreciate fully the advantages of good exposure through a posterolateral incision."

The anterior incision is excellent for an uncomplicated pneumonectomy or middle lobectomy. Since history and x-ray studies only suggest, but do not prove, that a case will be an uncomplicated one, it is the author's belief that perhaps the posterolateral approach with the patient placed either in the side position or suspended prone position is much to be preferred as a routine procedure in pulmonary excisional surgery.

Posterolateral Approach: Lateral Position. With the posterolateral approach the patient lies on the unaffected side, usually over a pillow to spread the ribs on the affected side. The pleural cavity is usually entered by resection of the sixth rib from the transverse process to the costal cartilage. Increased exposure may be secured by resection of small paravertebral costal segments from the ribs above and below. This is by far the position most frequently used, and this approach has become almost standard for pulmonary excisional surgery and for numerous other intrathoracic procedures. Intercostal incisions are quite satisfactory when properly used.

According to Sweet[3] the lateral position has a distinct advantage for pulmonary surgery in that it gives ready access to both the anterior and the posterior surfaces of the hilus of the lung.

However, the side position has many disadvantages. Overholt,[4] in his book on "Technique of Pulmonary Resection," has clearly enumerated the major disadvantages. In this position the diseased lung is uppermost, favoring contralateral spillage of secretions, blood and debris from the affected to the unaffected lung. If the discharges are excessive the bronchial tree will be flooded and the patient becomes literally drowned. Smaller quantities may occlude individual bronchi and predispose to patchy atelectasis. These secretions interfere with the administration of anesthetic agents and lead to postoperative complications.

X-ray films taken immediately following surgery in certain cases operated in the side position revealed in a number of instances multiple areas of focal atelectasis in the unoperated lung. In two cases, esophageal resection for malignancy and removal of a benign mediastinal tumor, the lung in the operated hemithorax was normal while the contralateral lung which was lowermost during surgery showed presumptive roentgen evidence of marked diffuse atelectasis, despite careful suctioning of secretions through the endortacheal tube during surgery by the anesthetist.

Lambert,[5] in the course of a roentgenologic study of the operated lung in resection cases for tuberculosis, found that the contralateral lung regularly showed evidence of poorer aeration than the operated lung; the hypoaeration being transient and usually clearing up in about five minutes on resumption of the supine position. He also emphasizes that the x-rays taken within three minutes following the termination of surgery while the patients were still under anesthesia and in the side position all showed multiple small areas of focal atelectasis in the contralateral lung.

In addition, when a patient is placed in the side position and the chest is open the respirations are impaired and the liability of anoxemia is increased because of the following reasons: (1) the lung in the open chest is partly or completely collapsed, (2) the patient's own weight restricts the expansion of the dependent normal side, (3) the mediastinal sag diminishes the volume of the sound lung, (4) periodic mediastinal shifting increases the chances of "Pendel-

luft" phenomenon, i.e., a purposeless and ineffective circulation of air in the lung of the affected side, and (5) the action of the dependent hemidiaphragm is hindered due to the weight of the abdominal viscera.

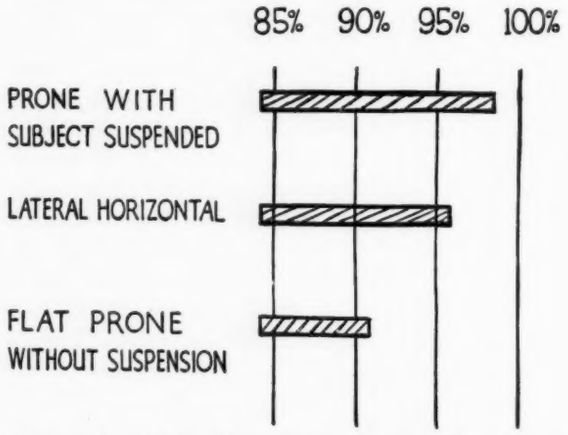

FIG. 1. Graph showing comparative ventilatory function in various positions; 100% represents normal ventilatory function in sitting position.

For these reasons, when the lateral position is used, either assisted or controlled respiration (high intermittent intrapulmonary pressure of the respiratory gases) by the anesthetist is necessary in the majority of transpleural operations and indispensible in a number of cases. However, these positive pressure methods may prove unphysiologic and undesirable if improperly used. They may result in (1) increases of carbon dioxide without notable clinical signs, (2) elevation of the peripheral venous pressure, (3) increase in the pulmonary arterial and venous pressure and (4) a decrease in the cardiac output.

In a recent panel Beecher emphasized that the lateral position is not the optimal position for the excretion of CO_2 without the aid of assisted respiration.[6] He is of the opinion that when the lateral position is used the occasional bad results, such as a puzzling condition of hypotension occurring at the end of the operation, may be directly related to the high carbon dioxide tension.[7]

In the previous article appearing in this symposium Pender and Lundy[8] discuss further the disadvantages of the lateral position and point out that the problems which are peculiar to the lateral position are known to all thoracic surgeons, but their extent and seriousness are not always appreciated.[5]

Posterolateral Approach: Suspended Prone Position. To overcome the disadvantages of the side position the use of the posterolateral approach, with the patient in the suspended prone position, has become more and more popular since its adoption and emphasis by Overholt and his associates.[9] This position has certain definite advantages. (1) With its use contralateral spillage is minimized and, in the presence of an abundance of secretions, the discharges gravitate to the outside through the endotracheal tube. In addition, the prone position facilitates aspiration of secretions by the anesthetist. These factors are of particular importance in disease with considerable intrabronchial suppuration. X-ray films taken immediately following surgery in numerous cases operated in the suspended prone position rarely revealed abnormal roentgen changes in the unoperated lung. Lambert similarly found no impairment of aeration or atelectasis in the contralateral lung with use of the suspended prone position.[5] (2) In tuberculous cases the high incidence of spread of active disease to the normal lung following resection has been decreased by employing the prone position.[10] (3) With the patient suspended in the prone position breathing is much easier and pulmonary function is markedly improved. The respiratory rates, vital capacity, tidal air, complemental and supplemental volumes, and maximal deep breathing were studied by the author in thirty normal, conscious, unpremedicated subjects in the following positions: right and left lateral recumbent, suspended prone and the flat prone without suspension. Of these the most favorable for pulmonary function is the prone with the subject suspended. (Fig. 1.) In this position, with the chest open, the mediastinum is suspended in its normal position and there is a minimum of shifting, thus permitting a full range of expansion of the normal lung. For these reasons the use of positive pressure assistance by the anesthetist is seldom necessary in the prone position.

Of the two great problems in thoracic surgery—oxygen supply and carbon dioxide removal—the usual technics are adequate to provide oxygen but not to remove carbon dioxide. In this regard Beecher has shown that in pneumonectomy cases operated upon in the suspended prone position the CO_2 remains at relatively normal levels even with no assistance.[11]

In the prone position additional advantages are those of exposure, (the approach to the hilum is considerably facilitated, the main bronchus is on top and may be easily and quickly treated with a minimum of disturbance to the lung, and the great vessels of the hilum are likewise easily approached); also, blood and irrigation solutions flow out of the wound by gravity. In addition, traction and the use of lung clamps are not necessary during dissection since the lung falls forward by its own weight. Since tension on the hilum is the chief cause of vagal reflexes, this probably explains why cardiac irregularities are practically eliminated in the prone position and why the need for injection of the vagus nerve with novocain® is rare.

This position may not be the one of choice for children; the thoracic cage not having reached its maximum growth and the osseous tissues including the sternum being soft and resilient, there exists the possibility of cardiac compression. X-rays taken during a lobectomy for bronchiectasis in a seven year old child revealed depression of the sternum and ribs. The author refers to this as the "Bamboo" phenomenon, occurring when an anesthetized child is placed in the prone position with the middle of the thorax (mid-sternum) resting on a support. However, the possibility of cardiac compression may be easily avoided if the clavicles and upper portion of the sternum are made to take the brunt of the weight.

Another disadvantage of the prone position may present itself when a surgeon operates with the patient at a low height level; difficulties may arise in that the anterior hilus may not be adequately handled. It has been reported to the author that an exsanguinating hemorrhage resulting from injury to the superior pulmonary veins has occurred due to inadequate exposure of the anterior hilus; and it was concluded that this constitutes a major disadvantage of the prone position. It must be emphasized that the region of the anterior hilus of the lung is as readily accessible in the prone position as in the lateral position if the surgeon allows himself to operate with the patient at a high height level.

Apparatus for Suspended Prone Position Surgery. Despite these and other advantages of the prone position, its use on a standard operating table has proved impracticable. When an anesthetized patient is placed face down on the firm flat surface of such a table, the vital capacity is appreciably diminished by the restriction of the diaphragmatic movements. This is a serious drawback, since the maintenance of respiratory function is dependent chiefly on the diaphragm while the thoracic muscles of respiration are paralyzed under surgical anesthesia. In view of this and the non-availability of an adequate device to suspend the patient in the prone position, the early use of the position resulted in numerous complications.

In regard to the aforementioned, in 1946 a series of apparatus were devised and experimented with by the author; the one proving to be thoroughly satisfactory is shown in Figure 2.[12] It is not an attachment to the table with incidental connections, but a separate unit in itself.* During this period the Overholt-Comper Thoracic Table was being designed for prone position surgery. Davidson later had a simple framework built which was an attachment for a conventional operating table; now called the Comper Frame. Hurley[13] had used firm pillows (8 by 8 by 18 inches) placed under the pelvis and across the manubrium of the sternum and clavicles.

However, regardless of the apparatus or method selected, greater care is necessary in positioning a patient for prone position surgery than when either the lateral or supine positions are used.

Since complications are still being reported with the use of the prone position, certain fundamental points relative to the positioning of the patient are mentioned. To obtain maximum efficiency with minimal ill effect to the patient, permitting free and unrestricted movements of the abdomen and major portion of the thoracic cage, the proper distribution of body weight must be achieved. This is dependent upon three variables: the angle of the chest (sternochondroclavicular) plate, the tilt of the operating table and the difference in height between the operating table and chest plate.

Excellent results are obtained with the patient in the position demonstrated in Figure 2. This shows a near-horizontal (slight angulated) chest plate and a difference in height between the pelvis and thorax of approximately 6 inches. By placing the operating table in slight Trendel-

* Manufactured by J. H. Emerson Company, Cambridge, Mass.

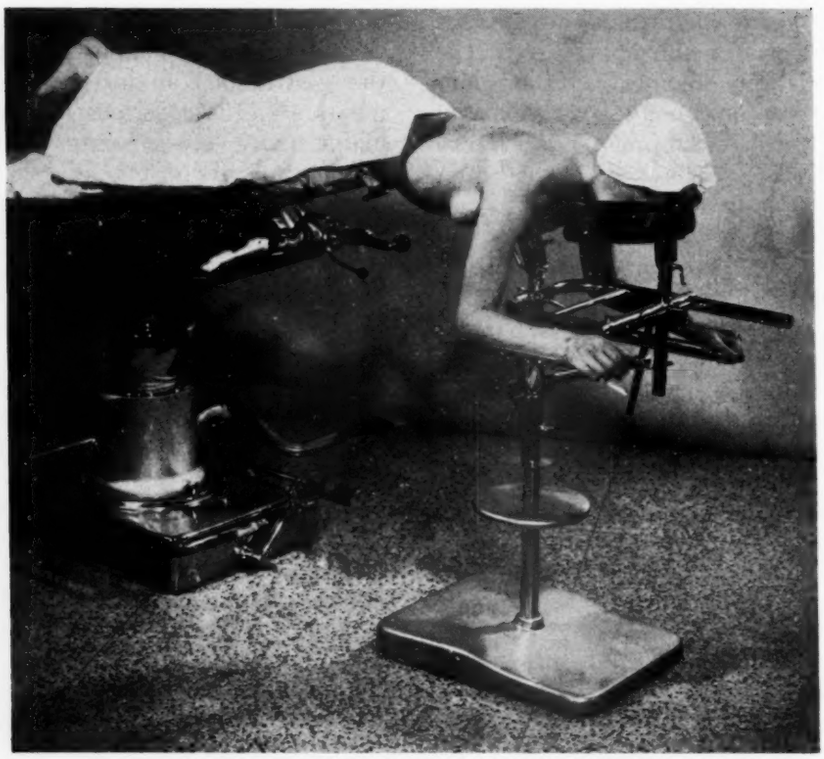

FIG. 2. Photograph demonstrating the support and standard operating table. The support suspends a part of the body while the pelvis and lower extremities rest upon the operating table.

enburg position, the weight of the body on the chest plate is greatly decreased. In addition, by raising the operating table to its maximum height excellent exposure of the anterior hilus of the lung is achieved.

The chest plate supports the clavicles and the upper part of the mid-thorax. It is notched anteriorly to coincide with the contour of the suprasternal notch of the patient. This enables the anesthetist to check the position of the patient with ease and accuracy during the course of surgery. To further prevent gravity spillage, if one belongs to that school of thought, the diseased lung may be tilted lower than the sound lung by positioning the patient slightly off center of the costoclavicular pad, and lowering the arm support on that side.

The headrest is horseshoe-shaped, well padded with foam rubber to eliminate the possibility of any pressure points and is fully adjustable so that any desired degree of flexion, extension or lateral rotation of the head and neck may be obtained. It supports the forehead and to a slight degree the cheek bones; the eyeballs are completely free. However, if desired, the positioning of the head may be altered; the side of the head may be placed on the rest. This will expose the entire face.

The entire apparatus rotates on its base. As the chest cavity is entered, the support is rotated to spread the ribs naturally. This is of particular value since wide and rapid spreading of the ribs by retractors may cause cardiac irregularities or arterial hypotension. This rotation also affords a most favorable approach to the apex of the lung and diaphragm. Chest closure is facilitated by rotating the support towards the surgeon and is of importance when a portion of the chest wall has been removed.

Complications Associated with Prone Position. Complications from the use of the suspended prone position have been reported, e.g., temporary unilateral or bilateral arm paralysis, low back pain, edema of the face and chest, mild hypotensive states, ocular injury, traumatic bruises of the skin and other complications incident to malposition on the operating table. With regard to these the author firmly believes that the complications are the result of makeshift arrangements. In addition contributing factors may be attributed to insufficient help, poor teamwork, hasty positioning

of the patient and inadequate knowledge as to the proper positioning of the patient.

Methods of Improving Ventilation and Circulation. With the patient in the suspended prone position the anesthetist is able to assist further ventilation and circulation by the use of an abdominal lifter.

That the movements of the abdominal contents can affect to a remarkable degree the ventilation of the lungs has been proved by Comroe and Dripps;[14] they showed that in the EVE rocking method of administering artificial respiration, the respiratory exchange was in the range of 280 to 500 cc. per cycle. In view of these observations and since it is known that the weight of the abdominal contents push and pull the diaphragm up and down like a piston, a method has been instituted for improving the ventilation in patients in whom the problem of pulmonary reserve is questionable.[15] In these cases the anesthetist is able to assist the respirations further by exerting pressure against the abdomen with an abdominal lifter. (Fig. 3.) Maximum ventilation is obtained when the lifter is raised during the latter phase of expiration and the anesthetist carefully correlates the lifting with each respiratory cycle of the patient. In a number of patients undergoing lobectomy and pneumonectomy in the suspended prone position it was observed that the respiratory exchange increased to a range of 100 to 200 cc. per cycle when pressure was exerted against the abdominal wall with the lifter.

In the occasional obese patient the use of the abdominal lifter will again prove helpful. In these cases splanchnic pooling of blood through sagging of the abdominal viscera may occur. By raising the patient's abdomen to the desired level, employing the technic already mentioned, the possibility of hypotension from splanchnic pooling is eliminated.

In the extremely obese patient in whom the weight of the abdominal contents and wall interferes with the respiratory exchange, the use of the abdominal lifter or some other type of partial support to the abdominal wall will prove of great value in improving ventilation. This has been attested to by careful observation of the tidal exchange during excisional surgery.[16]

FIG. 3. Photograph demonstrating a method of increasing the respiratory exchange in a patient in whom the problem of pulmonary reserve is questionable. Maximum ventilation is obtained when the abdominal lifter is raised during the latter phase of expiration and the anesthetist carefully correlates the lifting with each respiratory cycle of the patient.

SUMMARY

The author has attempted to evaluate the advantages and disadvantages of the suspended prone position as contrasted to the advantages and disadvantages of the lateral and supine positions. Data has been presented to show that normal pulmonary function is least disturbed by the suspended prone position. It has been shown further that during surgery, the dangers of contralateral spillage, hypoxia, carbon dioxide retention and respiratory fatigue are minimized by this position. In addition ideal conditions are obtained for optimum exposure. Since some surgeons still report complications resulting from the use of the prone position, the author has briefly described a specially designed apparatus which has proven thoroughly satisfactory in his experience.

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Surgical Principles Involved in Open Thorax Procedures

WITH SPECIAL REFERENCE TO PULMONARY RESECTION

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To obtain the desired surgical result in open thorax procedures the surgeon must avoid complications by the observance of certain basic principles. Attention to these principles is important in the surgical management of esophageal or cardiac diseases, but especially in pulmonary resection.

Ventilation. Ventilation, or the movement of air in and out of the lungs, is a variable respiratory characteristic. It is accomplished by diaphragmatic and costal movement, and because of senile emphysema and fixation of the thoracic cage in the aged, ventilation is reduced. In the young athlete ventilation reaches its maximum. After a thoracotomy there is some splinting of costal movement together with some diaphragmatic spasm to further reduce the ventilatory movement of air. This reduction is often significant in the patient with a low cardiorespiratory reserve.

Ventilation, in the movement of pulmonary secretions, is of great significance. The patient who moves air well moves secretions well, and in so doing maintains a patent tracheobronchial tree. Such patients rarely develop pneumonia, atelectasis or other postoperative complications. An effective cough is the sudden movement of air by which the patient protects himself against these complications. Therefore, before a thoracotomy is performed the surgeon must know the extent of the patient's ventilatory ability.

Ventilatory ability may be measured in a variety of ways. First, in the patient with ventilatory impairment, the history discloses some dyspnea or a tendency toward "asthma." In addition, on inspection of the chest the A-P diameter is increased, the ribs are horizontal, some kyphosis is present and the chest cage is fixed on inspiration and expiration. Percussion of the diaphragm posteriorly reveals slight, if any, detectable movement, and the patient appears to be in a state of permanent inspiration. Palpation confirms the aforementioned findings, but to classify each patient one must resort to auscultation.

Ventilation, on auscultation, is measured by the patient's ability to accentuate his breath sounds. All patients may be arbitrarily placed in one of four classes. In Class I we put the young athlete whose breath sounds are quiet while at rest but markedly accentuated on vigorous breathing. Such breath sounds are said to be excellent, and this patient tolerates a thoracotomy well without complications and with relatively little postoperative attention. In Class II the accentuation of the breath sounds is said to be good, and the patient is thought to be a good risk, but probably will require close postoperative attention if complications are to be avoided. In Class III the accentuation of the breath sounds is poor, the patient is a borderline risk and he will require constant and vigilant postoperative attention because of his inability to move air and therefore, secretions. These secretions may obstruct or occlude the smaller airways and establish a vicious circle of complications which is difficult to interrupt. Class IV presents little or no ability to accentuate the breath sounds. Each inspiration is almost the maximum inspiration for this patient. The quality of the breath sounds at rest and upon vigorous breathing is the same. In such cases no major thoracic surgical procedure can be successfully concluded unless the surgical objective results in functional improvement.

Ventilation during operation is the concern of the anesthetist. The tidal movement of air during an open chest procedure is accomplished by manual pressure on the anesthetic bag during inspiration. Some anesthetists prefer an automatic machine which can be adjusted to deliver the desired amount of tidal anesthetic mixture in a more accurate rhythmic fashion. One of the curare derivatives is used

at the same time to avoid asynchronous diaphragmatic costal movements. This automatic technic assures adequate and accurate ventilatory movement of the anesthetic mixture while the anesthetist performs other two-handed procedures, such as adjusting the intravenous fluids and blood, the recording of the patient's blood pressure and other details on the patient's chart, the removal of intratracheal secretions by intratracheal suction and the intravenous use of specific drugs in special cases or unusual situations. In patients properly ventilated during a thoracic procedure the oxygen and carbon dioxide tensions of the blood are essentially normal.

Ventilation after operation is reduced on the side of the thoracotomy because of the pain which leads to reflex spasm of the diaphragm and intercostal muscles. Hence, ventilation and breath sounds are reduced on the operated side. This reduction in ventilation is only significant when great as compared to the reduction of the pulmonary circulation. For example, after a subsegmental resection the reduction in ventilation may be great in a high-strung patient with a low threshold for pain. At the same time the pulmonary blood flow through the lung on the operated side may be only slightly reduced. Therefore, the blood returning to the left heart from the operated side may be low in oxygen and high in carbon dioxide content. In the left heart the blood returning from the unoperated side has normal oxygen and carbon dioxide tensions. The mixture is then distributed to the coronary and systemic circulations. In a young patient with elastic and widely patent coronary vessels the reduction in oxygen tension is easily tolerated. In older borderline cases the reduction in oxygen tension is an additional physiologic imposition upon the myocardium which may be a precipitating factor in cardiac failure. After a pneumonectomy the blood returning to the heart is from the unoperated lung and the oxygen and carbon dioxide tensions are, therefore, essentially normal.

Mediastinal "Flutter." Mediastinal flutter is the movement of the mediastinum during inspiration and expiration in an open chest. Mediastinal flutter implies instability, and in the early background of thoracic surgery an unstable mediastinum was frequently associated with death. As a consequence it was viewed with ominous regard in the historical memory of the thoracic surgeon. Now, however, with improvements in anesthesia the movements of the mediastinum can be easily controlled, so this fear has been removed.

Mediastinal movement before operation may be seen at fluoroscopy when air is trapped in one lung by partial obstruction of a major bronchus. Endobronchial tumors, foreign bodies or strictures are the usual causes of bronchial obstruction. When the bronchial lumen is almost completely obstructed and the patient is asked to breathe out quickly, air is trapped in the lung beyond the obstruction and the mediastinum quickly shifts to the opposite side. At fluoroscopy the lung or lobe in which the air is trapped seems to "light up," as compared with the relatively airless opposite lung.

Mediastinal movement at operation is dependent upon the difference of pressures within the two pleural cavities. These pressures vary with inspiration and expiration to influence the movements of the mediastinum. Mediastinal movements are slight when the diaphragmatic movement is slight, but the oxygen and carbon dioxide tensions of the blood may so influence the respiratory center that wide diaphragmatic excursions occur. At such times mediastinal movement or "flutter" is greatly accentuated during the respiratory cycle (inspiration and expiration).

Mediastinal "flutter" or movement may be reduced to insignificance by a competent anesthetist who assures the patient of an adequate tidal exchange of gases through intermittent pressure upon the anesthetic bag or, in other words, by assisting or supplementing the patient's efforts to breathe. It is of little or no value to inject the phrenic nerve with procaine on the side of operation hoping to obtain a "quiet" chest, since it is the opposite diaphragm and the size of its excursions that are mainly responsible for the mediastinal movements. Advocates of phrenic nerve injections are handicapped by poor anesthesia. Mediastinal "flutter" and the associated complications have been obviated by modern advances in anesthesia.

Mediastinal "flutter" after a thoracotomy is absent if the pressures in the two pleural cavities are essentially the same. However, after thoracoplasty when too many ribs have been removed, the pressures of the two chests become unequal and mediastinal "flutter"

occurs almost as though the chest were open to atmospheric pressures. Mediastinal "flutter" under such conditions is referred to as paradoxic breathing. In the standard thoracotomy during which one rib is removed and perhaps two others are divided posteriorly, the intrapleural pressures are such that little or no movement of the mediastinum can be detected at fluoroscopy after operation.

Surgical Exposure. The posterolateral incision is the incision of choice in the majority of thoracic procedures. All pulmonary and esophageal surgery and much of the cardiac surgery can be done best through this incision. The anterolateral incision for pulmonary operations is a challenge to the most skillful surgeon. The anterior approach was popular in the early development of thoracic surgery, because it was fast and there was less mediastinal "flutter." Now, with the advances in modern anesthesia which easily control mediastinal movements, time is sacrificed for better exposure. The surgeon who has encountered severe hemorrhage in an open chest can fully appreciate the advantages of good exposure through a posterolateral incision.

Through the posterolateral incision a long segment of one rib is usually removed and two others (one above and one below) are divided near the transverse processes posteriorly. Intercostal incisions are equally satisfactory when the intercostal muscles are divided precisely halfway between the two ribs. The two ribs should be divided near the transverse processes posteriorly to attain better exposure and to prevent fractures of the ribs in undesirable locations as the rib spreader is opened. In closing the intercostal incision interrupted sutures are placed in the intercostal muscles, but not tied until the Bailey rib approximator has returned the ribs to their normal position. They are then tied and upon removal of the Bailey instrument, the strain is shared by all the sutures at once.

Drainage. Drainage of the pleural cavity is used as a safety measure after every major thoracotomy to prevent postoperative complications. If instituted at the time of operation, tube drainage averts the necessity of needle aspiration later on. Needle aspiration, of course, requires the presence of a doctor, a nurse and a third person to clean and sterilize gloves, sheets, needles, stopcocks and syringes after the procedure, whereas tube drainage requires only an additional five minutes at the operating table and five minutes for the removal of the tube forty-eight hours later. Tube drainage, in addition to its other advantages, is a labor-saving measure.

The pleural cavity is drained to prevent infection. A method of aseptic anastomosis of the esophagus and stomach or of closure of the bronchus has yet to be devised. Consequently, it must be assumed that the pleural cavity has been contaminated by the flora of the oral cavity in all cases. Moreover, since there is always some blood and air left in the pleural space after operation, the pleural cavity may be thought of as a culture tube within the body which provides ideal temperatures for the incubation of bacteria. Tube drainage removes most of the blood and maintains re-expansion of the lung, thereby obliterating dead space, a basic surgical principle in the prevention of infection.

Drainage of the pleural cavity also prevents the accumulation of blood which, if unattended may necessitate decortication of the lung later on. Thus, every major thoracotomy must be treated as a hemopneumothorax, for which tube drainage provides the most convenient solution.

Drainage of the pleural cavity prevents the development of a tension pneumothorax and the subcutaneous emphysema which is often associated. After a lobectomy, in which the fissures have been undeveloped, or after a segmental resection air escapes through many small alveolar openings. This situation is comparable to the leakage which occurs after the development of a spontaneous or traumatic pneumothorax. The accumulation of air in the pleural cavity or its dissection into the subcutaneous tissues, which might also occur, may be prevented by tube drainage and rapid suction.

Drainage of the pleural cavity will maintain re-expansion of the lobe or lung and preserve pulmonary function. A partially collapsed lobe or lung is not well ventilated. Consequently it acts as a blood shunt, from which blood returns to the heart low in oxygen and high in carbon dioxide. Furthermore, if re-expansion is good and an empyema should develop, the size of empyema will be small. It follows that if an empyema develops with the lung markedly collapsed, the empyema will be large and the corrective procedure proportionately large.

Drainage of the pleural cavity is performed to control the intrapleural pressures. As blood and fluid accumulate in the pleural cavity after pneumonectomy, the air left in the pleural cavity is compressed. A positive pressure is then developed which may move the mediastinum toward the opposite chest, and if sufficiently high, may interfere with the flow of blood returning through the vena cava. Usually, however, water seal drainage is not used after pneumonectomy because coughing and straining during anesthetic recovery expel so much air from the pleural cavity that a high negative pressure develops. The mediastinum then moves too far toward the operated side, displacing the heart and overdistending the opposite lung. As a result, the normal cardiophysiology may be seriously disturbed, especially after a right pneumonectomy. A small, clamped catheter left in the first interspace is preferable. This catheter may be opened at the end of an expiration every two or three hours after operation to allow the escape of air. Before the following inspiration the tube is quickly occluded to establish a normal negative pressure on the operated side. Under these conditions the mediastinum and its structures remain in the midline. The tube may be removed on the second day after operation since the rates of fluid formation and air absorption equalize in forty-eight hours.

Fluid Administration. Blood should be replaced as it is lost. Most major thoracic procedures of surgical nature require 2,000 cc. of blood. The speed of administration should vary with the amount of bleeding, but 500 cc. per hour of surgery is an average rate of flow. Excessive use of blood is as hazardous, for well known reasons, as the excessive use of fluids. If intravenous glucose is used in addition to blood on the day of operation, 1,000 cc. usually is sufficient and this is administered in distilled water and very slowly. In general, if it is necessary to use intravenous glucose in the first few postoperative days, it is better to err on the side of dehydration, especially with older patients.

Antibiotic Therapy. Antibiotic therapy is no substitute for attention to surgical principles, but the combination of good surgery and antibiotic therapy has increased our surgical successes. If a pulmonary infection is present, antibiotics should be used preoperatively until the sputum has been reduced to a minimum and the clinical picture has improved to a maximum. Therefore, an accurate daily examination of the character and amount of sputum is essential.

Antibiotics are particularly useful in improving oral hygiene. The fact that acute infections of the lung are rare in the edentulous patient is important. Lung abscess, aspirational pneumonia and postoperative complications are seldom found in patients without teeth. Their mouths are relatively sterile. Low grade sinus infections must also be considered and are improved by the preoperative use of antibiotics. It follows, therefore, that all patients should have dental consultations and an adequate preoperative course of antibiotics in preparation for a major thoracic procedure. It is perhaps justifiable to add for emphasis the comment that at some time during an esophageal or pulmonary resection the patient spits in his own pleural cavity; hence the attention to oral hygiene.

Antibiotic therapy during and after surgery is equally important and should be continued as long as seems necessary. In tuberculosis the use of streptomycin may be continued for several weeks or months.

SUMMARY

1. Ventilation, or air movement, determined before operation is usually proportional to lung function. The patient who can move air well has few postoperative complications because the cough is effective to maintain patent airways. Ventilation is easily determined by listening to the patient's breath sounds at rest and comparing them with the sounds during vigorous breathing. The Class I young athlete who can accentuate his breath sounds markedly during vigorous breathing is in distinct contrast to the Class IV emphysematous old man whose costal and diaphragmatic fixation prevents air movement and therefore the accentuation of breath sounds. Class I, II and III patients are surgical candidates. Class IV patients are not.

2. Mediastinal "flutter" is a complication of poor anesthesia. It is rarely seen today except as a result of trauma on the battlefield or of an automobile accident. Its presence at thoracotomy is due to the violent excursions of the opposite diaphragm. It cannot be controlled by the injection of the phrenic nerve on

the operated side. A quiet opposite diaphragm implies normal oxygen and reduced carbon dioxide tensions of the blood. This is accomplished by the anesthetist's using an automatic machine, or by intermittent pressure upon the anesthetic bag synchronous with inspiration. Mediastinal "flutter" after a thoracoplasty is in direct proportion to the number of ribs removed. Staged procedures will avoid its complications.

3. In thoracic surgery adequate exposure is best obtained by use of the time-consuming posterolateral incision. In difficult cases adequate exposure may be paramount to the control of accidental hemorrhage. The living time saved any one such patient more than compensates the surgeon for the time lost from his career.

4. Antibiotic therapy is no substitute for, but is an established adjunct to, basic surgical principles. Its use in preparing some cases for surgery is often more important than its use after the operation.

5. Blood is replaced as lost at an average speed of 500 cc. per hour of surgery. The apparatus for arterial transfusions should be available in cardiovascular surgery, but the excessive use of blood and fluids is to be discouraged in pulmonary resections. Mild dehydration is preferable to excess fluid.

6. Drainage accomplished by the use of one or two intercostal tubes not only assures reexpansion and the preservation of lung function, but is a labor-saving device for the nurses, house staff and attendants who must otherwise prepare for, assist at and clean up after each needle aspiration of the chest. Furthermore, tube drainage helps to avoid infection, empyema, hemopneumothorax, subcutaneous emphysema, "trapped lung" and the associated corrective surgery. Drainage of the pleural cavity after pneumonectomy is a specialized problem.

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Cardiac Arrest during Pulmonary Resection

ETIOLOGIC FACTORS AND MANAGEMENT

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THERE is nothing more catastrophic than a sudden unexpected death in the operating room. This is true whether the operation being performed is a pulmonary resection or a less extensive procedure. It is particularly unfortunate when the patient is young and the lesion is benign. Under such circumstances it is a normal reaction for the family to assume that the surgeon has made some error to account for the patient's death. However, unless the surgeon has encountered uncontrollable hemorrhage, the cause of the death may not be readily apparent. A few years ago the family was told that the patient "did not take the ether well." Today the family is told that the patient died of cardiac arrest.

In recent years there has arisen a widespread interest in cardiac resuscitation. We would be the last to say that we should not continue to do everything in our power to maintain this interest for we have expended a great deal of effort toward helping to create it. On the other hand, it would now seem to be time to shift our emphasis toward the prevention of cardiac arrest.

INCIDENCE

At the Hospital of the University of Pennsylvania there have been approximately 108,000 operations performed in the last eight years. There have been thirty cardiac arrests in the operating room, or an incidence of 1 in 3,600. If the twelve patients subjected to cardiac surgery are excluded, so as to make the figures more nearly applicable to most general hospitals, there have been eighteen patients with cardiac arrest in the operating room, or an incidence of about 1 in 6,000 operations. While only one of the patients was in the pulmonary resection group, three others developed cardiac arrest at about the time of intubation or extubation. It should be pointed out that the figures given here do not include deaths from cardiac arrest after the patients have left the operating room. Also, deaths in the operating room due to hemorrhage or other obvious causes are not included.

ETIOLOGY AND PREVENTION

A major objective at present is to learn more about the causes of cardiac arrest so that we may prevent it.

1. One obvious cause is an overdose of the anesthetic agent.[1] There are those who say that cardiac arrest is much more common now, since we have medical anesthetists who use multiple anesthetic agents, than in the old days when we had nurse anesthetists giving open drop ether. That may well be true but it must be remembered also that much of the surgery which we are doing today could not be done in the old days under those conditions. Moreover, many of us can remember deaths in the operating room in the old days when "the patient didn't take the ether well."

No one can deny that the patient having her gallbladder removed is safer with a nurse anesthetist with perhaps twenty to thirty years' experience in giving open drop ether, than with the resident medical anesthetist perhaps in his first year of training who gives spinal anesthesia and then, when that doesn't work well, supports it with some intravenous pentothal, a little nitrous oxide, cyclopropane and ether, and perhaps a bit of curare for adequate relaxation—not to mention half a dozen other drugs to make the patient's blood pressure go up or down. We do not wish, by this remark, to depreciate the contributions made by the outstanding physicians who have developed the field of anesthesiology. As thoracic surgeons, we are acutely aware of the important role played by anesthesiologists in

the development and progress of our specialized branch of surgery.

Nevertheless, an overdose of anesthetic agents is a very frequent cause of cardiac arrest. Our medical anesthetists must accept that responsibility. The choice of the anesthetic agent and the judgment as to dosage are highly important. When multiple agents are used, the difficulty of judging dosage may be compounded.

The surgeon is not entirely free of responsibility when it comes to an overdose of the anesthetic agent. When he is in a hurry and presses for more relaxation, the inexperienced anesthetist is apt to give too much of too many agents in an effort to please his surgeon quickly.

The only way to prevent this common cause of cardiac arrest is to provide better training for our medical anesthetists. There are those who believe that it would be a wise plan to teach the young man to use one agent well and after he had mastered that to add another and so on. It seems very likely that the agent is not too important if it is used well, and that it is better at first to train the anesthetist thoroughly with one agent than to throw the whole pharmacopeia at him at once. This matter of overdosage is the problem of the anesthetist, however, and he must accept it.

2. A second very common cause of cardiac arrest is hypoxia. Even when it is not the primary cause, it may be a contributing cause. Ether is such a strong respiratory stimulant that in the old days the patient was not apt to suffer from severe hypoxia unless he had an obstructed airway or was given an overdose. With the advent of thoracic surgery and the open chest, the anesthetists took on a new responsibility—that of providing adequate ventilation of the lungs so as to keep the patient oxygenated and to eliminate the CO_2. It has now been repeatedly shown that an accumulation of CO_2 and a deficiency of oxygen are common causes of cardiac arrest.[2] Much has been written in the anesthesiology literature as to the best position of the patient for adequate ventilation, and as to controlled respiration versus assisted respiration. Let there be no doubt, however, that adequate ventilation is required regardless of the method by which it is obtained.

A high spinal anesthesia may paralyze the muscles of respiration,[3] and the more recent curare-like drugs may stop respiration completely. For this reason, adequate ventilation has now become a problem even in abdominal surgery. These factors and, upon occasion, the inadequacy of the anesthetist in coping with them, have undoubtedly increased the incidence of cardiac arrest.

The surgeon is not without responsibility as to adequate ventilation of the patient. If the blood is inadequately oxygenated, he should be the first to recognize it. Moreover, he should drape his patient so that the anesthetist can watch the wound for evidence of cyanosis. During a pulmonary resection the patient should be draped so the anesthetist can watch the lung to see its movement and help judge the adequacy of the ventilation.[4] In general, more trouble has arisen because of inadequate ventilation than any other one thing. It is far better to hyperventilate the patient than to carry him along on minimum ventilation.

With a poor risk patient ventilation should not be stopped for long periods while the anesthetist takes the blood pressure, writes on the chart, fixes the light and does many other things. During operation on a poor risk patient two people should be at the head of the table so that ventilation may be continuous. Even in the good risk patient we encourage our anesthetist to hold his own breath when he stops ventilating the patient to do other things. Under such a regimen we have been pleased with how much more quickly the anesthetist returns to ventilating the patient and how he may even use hyperventilation for a bit to make up for the time lost.

3. Apparently the heart sometimes stops as the result of the vagovagal reflex.[5] There is evidence to suggest that vagal stimulation is much more apt to produce this catastrophe in the presence of hypoxia.[2] In any event, cardiac arrest frequently occurs during intubation or extubation of a patient.

It would seem obvious therefore that the patient should be well oxygenated before the endotracheal tube is to be inserted or removed and that the trachea should be traumatized as little as possible.

In the early days of thoracic surgery a great deal was written about reflex stimuli caused by the surgeon during his dissection around the hilum of the lung. At one time it was common practice in some clinics to inject procaine solution around the hilar structures before starting the dissection. As far as we know, this practice

has been largely abandoned. As long as the patient is well oxygenated and the surgeon uses care in dealing with the mediastinal structures, the vagovagal reflex probably will not constitute a problem during that phase of the operation.

4. In all probability most instances of cardiac arrest are the result of a combination of factors. The surgeon should be particularly careful to prevent sudden loss of large amounts of blood and should avoid undue traction on the viscera in either the abdomen or thorax.

The cardiac surgeon may cause cardiac arrest by direct stimulation of the heart. This is almost always in the form of ventricular fibrillation. Much has been done in an effort to prevent these catastrophies. For a long time we, along with others,[6] used quinidine, procaine and procaine amide in an effort to prevent these irregularities. We have come to believe, however, that adequate oxygenation of the myocardium and gentle handling of the heart, along with minimum anesthesia and maximum blood flow, are the best preventive measures.

DIAGNOSIS

Time is the most important factor in the successful management of cardiac arrest, for the blood flow to the brain may be interrupted for only about four minutes if the patient is to survive. With such a short period of time in which to revive a patient, it is obviously highly important to recognize when that four-minute period begins.

The thoracic surgeon is in a very favorable position during a pulmonary resection for if cardiac arrest should occur during the course of the operation, it will be noted immediately. If the chest has not been opened or if the operation is not in the thorax, the surgeon is to a considerable extent dependent upon his anesthetist to ascertain a sudden cessation of blood flow. This requires constant and careful observation by the anesthetist. It goes without saying that if the anesthetist feels the patient's pulse only every four or five minutes it would be possible not to recognize the cardiac arrest until it was too late to do anything about it. It is evident therefore that the anesthetist must maintain constant observation of the patient if he is to notice an abrupt failure of the circulation the moment it occurs.

When the anesthetist observes that the pulse and blood pressure have suddenly and unexpectedly disappeared, we must assume that cardiac arrest has occurred, even though the question may arise as to whether the heart is still beating but so feebly as to be undetectable. Even when the surgeon is operating in the thorax, he may not have the heart in full view and may not note the arrest until his anesthetist calls it to his attention. Fortunately, however, the diagnosis can be confirmed or denied immediately. Likewise, when operating in the abdomen, the surgeon may immediately feel the heart through the diaphragm or feel for a large artery. When less exact methods of confirming the diagnosis are employed, fatal delay may be the result. Time spent looking for a stethoscope if one is not immediately available is time ill spent, since a heart beating so feebly as to produce no pulse or blood pressure is not apt to be heard anyway.

If an electrocardiograph happens to be attached to the patient, ventricular fibrillation may be diagnosed the moment it occurs. In the presence of ventricular asystole, a profound change in the electrocardiogram will also occur. But if an electrocardiograph is not already attached to the patient, fatal delay can be the only result of taking the time to attach it.

It becomes obvious therefore that the only reliable rapid method of determining whether the patient has cardiac arrest, unless the patient has an electrocardiograph or some similar apparatus attached at the time, is to see or feel the heart or a large artery. We are convinced, therefore, that the surgeon should take the point of view that opening the thorax to feel the heart is a diagnostic procedure.[7] If the anesthetist suddenly and unexpectedly cannot obtain a pulse or blood pressure, the surgeon must accept his observation and open the chest without losing valuable time in attempting to confirm these observations or to make a diagnosis of cardiac arrest by time-consuming and perhaps unreliable diagnostic methods.

It goes without saying that if an anesthetist or surgeon has never thought through what he would do under such a circumstance, it is extremely unlikely that he can do so sufficiently quickly to save a life. This is no time for meditation or consultation. Once it is found that the pulse and blood pressure have suddenly and unexpectedly disappeared, the surgeon should be prepared to open the chest with the greatest dispatch. He needs only a

scalpel. If sterile gloves are immediately available, perhaps he may take time to put them on but not otherwise. Skin antiseptics and sterile drapes are refinements which can be added later. Their absence should not cost the patient his life. It is far better to have a live patient with an infected wound, than a dead patient with a sterile one.

Given a scalpel, the surgeon should have his hand on the heart in ten or fifteen seconds. The incision should be made in the fourth or fifth interspace. If there is no bleeding, the diagnosis is confirmed. If there is bleeding, the incision need not be carried into the chest. The knife should not be plunged through the chest wall with one stroke for fear of cutting into the heart. Having cut through the skin and muscles, the final opening in the pleura should be made with the handle of the knife or with a finger to avoid cutting the lung. The interspace may then be opened widely while the left hand protects the lung. The hand may then be pushed between the ribs and compression of the heart started. The cartilages above and below may then be cut to allow more room.

TREATMENT

In the treatment of cardiac arrest it is not important to differentiate between ventricular asystole and ventricular fibrillation at the outset. The emergency problem is to establish artificial respiration and artificial circulation so that oxygenated blood may immediately go to the brain. If there is cardiac asystole on the basis of the vagovagal reflex, the heart will resume normal activity as a rule after a few moments of rhythmic compression. If there is a cardiac asystole on the basis of an overdose of anesthesia, it is a simple problem of maintaining the artificial respiration and circulation until the excess anesthetic agent is removed or detoxified. If hypoxia is the problem, the circulation of well oxygenated blood is all that is required. The important thing is that circulation must be restarted before there is irreparable brain damage. If the heart is in ventricular fibrillation, other considerations in treatment are usually required, but they come after the tissues are oxygenated.

RESPIRATION

If the emergency arises in the operating room, artificial respiration will be provided by the anesthetist. If an endotracheal tube is already in place it, of course, will be used. If not, ventilation can be obtained with a face mask until the patient is well oxygenated before taking time to insert an endotracheal tube.

If the emergency should arise outside the operating room, the patient's lungs may be ventilated by mouth-to-mouth breathing or an emergency device[8] until other equipment becomes available.

CIRCULATION

While the anesthetist is accustomed to providing artificial respiration for the patient, the surgeon is not accustomed to providing artificial circulation, which is equally essential if the patient is to survive.

As soon as the surgeon has his hand upon the heart and finds it is not beating, he should start compressing it rhythmically. A rib spreader or even hand retractors are helpful, when available.

There are a number of factors which greatly influence the effectiveness of the blood flow produced by cardiac massage.

Technic of Cardiac Compression. In the laboratory[9] it was found that some practice was required to produce an effective blood flow by cardiac massage. The dog's heart may be compressed most effectively by placing the thumb in front of the heart and the fingers behind it. The blood flow produced by compressing the heart against the anterior chest wall was only about half as great as by the foregoing method, while only one-fifth as much blood flow could be produced by compressing the heart through the diaphragm.

A small human heart may be compressed with one hand in the same manner as the dog's heart. A large human heart may be compressed more effectively with less effort, perhaps, by placing one hand in front and one hand behind the heart. The effectiveness of the cardiac compression may be judged by the pulse and the improvement in the color of the patient's skin and tissues. If a good pulse is not palpable at the wrist with each cardiac compression, something is wrong.

There are those who think that the pericardial sac should be opened routinely to improve the effectiveness of cardiac massage. We do not agree with this. Certainly time should not be taken to open the pericardium initially. It is wise perhaps to dissect into the anterior mediastinum in order to get around the heart

more effectively during compression. The pericardium serves to protect the heart from trauma. If the heart does not respond early and the ventricles cannot be felt to be fibrillating through the pericardium, it may be opened to visualize the ventricles directly. Subsequent massage should be done with the flat palms of the hands and not with the fingertips. We have seen not only the auricles but the right ventricle torn by the fingertips. If the heart has been massaged for a long time even through the pericardium, it is probably wise to leave an opening in the pericardial sac to allow drainage of any blood or fluid which may collect as the result of trauma.

Rate of Cardiac Compression. There has been some difference of opinion as to the rate at which the heart should be compressed. Some recommend a rate of twenty to forty times a minute to allow the ventricles to fill better during diastole. We and others have advocated a faster rate. In dogs we found that the blood flow increased as the rate of cardiac compression increased, regardless of whether the heart felt full or empty. Rates of thirty, sixty and 120 times per minute were used and in all instances the flow increased as the rate of compression was increased.[9]

For practical purposes there is a limit to the rate of cardiac compression which can be maintained by the surgeon. If a single surgeon is available, it is difficult to maintain more than sixty compressions per minute for a long period of time. If two or more are available to alternate, a rate of eighty to 100 or higher can be maintained to advantage.

Blood Volume. In the laboratory, when the dog's heart felt empty, the cardiac output could be significantly increased by a rapid transfusion of blood or a plasma substitute. In clinical practice care should be taken not to allow the blood volume to be depleted. This can be recognized when the heart feels empty in spite of waiting a second or more for it to refill. However, equal care must be exercised in not overtransfusing such a patient.

Diversion of Blood Flow. If there is reason to believe that the blood flow being produced artificially is inadequate, it may be wise to clamp or compress the descending thoracic aorta, thereby forcing more blood to the brain and coronary arteries. This, of course, should not be done for any prolonged period of time. In the laboratory, the blood flow to the carotid arteries could be greatly increased by occluding the descending aorta.[9]

DRUGS

Drugs appear to have no value in getting the heart to start beating again. Once the heart starts to beat, however, some drugs may be helpful in increasing the forcefulness of the contractions. Epinephrine at times appears to be very effective and calcium chloride also has been of considerable help in some patients.[10] In some cardiac patients we have also found vasoconstrictors such as nor-epinephrine, vasoxyl, neosynephrine and the like to be of great value. For a time we used procaine routinely in patients with asystole, hoping to prevent ventricular fibrillation. We no longer do so because of its deleterious effect on the blood pressure and effectiveness of the heart beat.

VENTRICULAR FIBRILLATION

The presence of ventricular fibrillation may often be diagnosed the moment the hand is placed on the heart because of the irregular contractions of small segments of ventricular musculature. On the other hand, the fibrillary twitchings may be occurring in such small segments of the ventricular muscle that they are not obvious by palpation alone. It is wise therefore to suspect that the heart is in ventricular fibrillation in every instance in which it does not return to normal rhythm after it has become well oxygenated. Direct inspection of the heart after opening the pericardial sac will give the answer. It should be remembered, however, that the appearance is quite different when the ventricles fibrillate in large segments as opposed to small segments.

The usual causes of ventricular fibrillation are hypoxia, mechanical trauma, electric shock and drugs which increase the irritability of the heart. Clinically, ventricular fibrillation is commonly due to coronary occlusion, or respiratory obstruction during anesthesia. In recent years ventricular fibrillation has also occurred commonly as the result of operations directly upon the heart.

In rare instances ventricular fibrillation has reverted to normal rhythm spontaneously or following the use of procaine.[11,12] In most instances electric shock as developed by Wiggers[13] and Beck and Mautz[14] must be employed. This method of treatment is based upon the observation that the passage of a

strong electric current through the heart will cause a simultaneous contraction of all heart muscle fibers. Following this contraction, the heart is in standstill as relaxation follows. The spontaneous heart beat will then return in regular rhythm after a short period of asystole.

Before defibrillation is attempted, anoxia must be overcome by cardiac massage and ventilation of the lungs with 100 per cent oxygen. The color of the myocardium should be returned to a near normal color. It is seldom profitable to shock a cyanotic heart. The amount of current to be used depends upon the size of the heart. When dealing with a child's heart, 110 volts for 0.10 second will usually suffice. The same current may be used initially for an adult heart of normal size. For hearts which are greatly enlarged as the result of heart disease, stronger currents may be necessary. We have recently found in the laboratory that stronger currents may be safely used if the duration is limited with a timing device.[15] If a single shock is not effective, repeated shocks (serial defibrillation) may be necessary.

In using the electric defibrillator it is important to remember that it is theoretically possible to electrocute the operator and proper precautions should be taken. The handles to the electrodes should be insulated but even so it is probably wise for the operator to wear two pairs of rubber gloves. The isolating transformer now present in all defibrillators is an added protection since the operator must come in contact with both electrodes to receive a lethal shock. Even so, it may be wise to avoid contact with the metal operating table and to stand on a wooden stool while applying the shock. Assistants and anesthetists should take their hands off the patient and operating table as the current is applied.

CLINICAL EXPERIENCE

Cardiac arrest, which may be divided into ventricular asystole and ventricular fibrillation, is a catastrophe which may occur from time to time on any active surgical service. Reports of our experience have been made periodically.[16,17] The present report is confined to the Hospital of the University of Pennsylvania during a period of eight years from January 1, 1946 to 1954.

During this time approximately 108,000 operations have been performed with thirty cardiac arrests in the operating room. Twelve of these were in cardiac surgical patients. This gives an incidence, as previously noted, of one in 6,000 operations, not including cardiac cases, or one in 3,600, if all cases are included. Only one-third of the cardiac cases have been successfully resuscitated while one-half of the general cases have ended successfully. In only one instance in this series did cardiac arrest occur during pulmonary resection. That was in a twelve year old boy undergoing lobectomy for bronchiectasis. Asystole was noted immediately and regular rhythm returned promptly after a few moments of massage. Recovery was complete. The asystole occurred while a pleural flap was being elevated to cover the bronchial stump. The vagovagal reflex may have been a factor. The authors have also experienced one other cardiac arrest during pulmonary resection in another hospital, and this is not included in our statistical data. In that instance the arrest was noted because although there was bleeding as the skin was incised, there was no bleeding as the muscle was incised. The incision was quickly carried into the chest and the heart returned to normal rhythm after a few manual compressions. The proposed lobectomy was carried out and recovery was complete.

TABLE I
CARDIAC RESUSCITATION EXCLUDING PATIENTS FOR CARDIAC SURGERY

Year	'46	'47	'49	'49	'50	'51	'52	'53	Total
Attempts	1	2	1	2	2	3	2	5	18
Successes	0	1	0	2	2	1	1	2	9

TABLE II
CARDIAC RESUSCITATION IN PATIENTS FOR CARDIAC SURGERY

Year	'46	'47	'48	'49	'50	'51	'52	'53	Total
Attempts	0	0	0	1	2	1	2	6	12
Successes	0	0	0	1	2	0	0	1	4

Our experience, excluding cardiac cases, is shown by years in Table I. The cardiac cases are shown in Table II.

As the experience in this hospital has grown, the concept of opening the thorax quickly in cases of suspected cardiac arrest has been repeatedly stressed to the personnel of the departments of surgery and anesthesiology. As a result several of the patients owe their

lives to the quick action of resident surgeons who opened the chest upon the advice of the anesthetist without waiting for consultation. In almost every instance in which resuscitation was unsuccessful in the general group, the failure could be attributed to delay. Two of our failures in 1953, for example, were in orthopedic patients in body casts. Valuable time was lost in removing enough of the body cast to get at the heart. One of these children existed as a decerebrate specimen on our wards for fourteen months before dying.

In the general group of patients (excluding cardiac patients) the heart was usually found in standstill. Almost without exception, the heart either returned to normal rhythm or went into ventricular fibrillation. With few exceptions the heart could then be defibrillated by electric shock after it was well oxygenated. In the failures the patients then went on to die of brain damage or their hearts did not continue to beat effectively. Almost without exception failure could be attributed to too great delay.

In the cardiac patients ventricular fibrillation was apparently due to direct stimulation of the heart either by a cardiac catheter, as occurred in two patients, or during an operation upon the heart. In the two instances of cardiac catheterization an electrocardiograph was running at the time so that the diagnosis of ventricular fibrillation was made immediately. These catheterizations were being done by medical men, and even though there was some delay in getting a surgeon and mouth-to-mouth breathing was employed for ventilation, both were successfully defibrillated.

Of the ten patients in whom ventricular fibrillation developed during cardiac operation, all but one could be defibrillated. The others were returned to their beds, but only two survived to leave the hospital. The others died from two to thirty days later. In no instance was there any evidence of brain damage, because there was no delay in beginning resuscitation.

In this report we have not included the attempts at cardiac resuscitation outside of the operating room where the delay in diagnosis and treatment is difficult to overcome because the patient may not be observed constantly. We have had no successes under such circumstances. One try at cardiac resuscitation outside the operating room was successful for thirty days but the patient died before leaving the hospital. In this instance a surgical resident happened to be at the bedside when the ventricular fibrillation occurred.

It would seem perfectly obvious that the most effective method of dealing with cardiac arrest is to prevent its occurrence. It is equally obvious that when it does occur many of the patients may be revived by prompt action on the part of the anesthetist and surgeon.

SUMMARY

1. The methods and technics which have proved successful in resuscitating patients with ventricular asystole and ventricular fibrillation are discussed.

2. Success in cardiac resuscitation depends upon the restoration of the flow of oxygenated blood to the brain within about four minutes. All other considerations are of secondary importance.

3. All surgeons and anesthetists should became familiar with the technic of cardiac resuscitation since the limitations of time do not allow for consultation should the emergency arise.

4. During an eight-year period thirteen patients have been successfully revived at the Hospital of the University of Pennsylvania following sudden death in the operating room.

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Pre- and Postoperative Care in Pulmonary Surgery

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OPENING of the thorax, whether it involves an attack upon the lungs, heart, aorta, esophagus or mediastinum, imposes special problems in the care of a patient if the surgeon is to insure safe conduct of the patient through the preoperative, operative and postoperative period. Correction of metabolic disturbances, abnormal losses of fluids and electrolytes, and problems of intestinal mobility and continuity are uncommon in thoracic surgery except in esophageal lesions; the prevention and treatment of shock is entirely comparable to that in general surgery, recognizing that blood loss is often more extensive in thoracic procedures; and the control of infection and preservation of pulmonary or cardiac function offer special problems in the postoperative management related to expansion of the remaining lung and altered cardiac compensation. Pulmonary and esophageal surgery has passed through the initial phase of rapid growth and its technics are quite well standardized; new horizons are being vigorously explored in cardiac and aortic surgery, employing new technics such as hypothermia, by-pass of the circulation, and others which are beyond the scope of a general discussion. It is proposed to focus the attention of this paper on the general problems of care common to the majority of pulmonary surgical procedures.

Preservation of pulmonary function and the prevention and treatment of infection are inseparable problems in pulmonary surgery. The rigidity of the chest wall imposed upon the lung the necessity of filling the thoracic space. Failure of the lung to expand and fill completely the volume of the thoracic cage permits the development of a "dead space" within the thorax, a space lined on the outside by the rigid thoracic cage and on the inside by a tough fibrinous membrane. Such a "dead space" predisposes to infection and its chronicity is almost inevitable from the nature of the involved space. On the other hand, attempts of an insufficient amount of pulmonary tissue to overexpand and equal the thoracic volume may predispose to breakdown of the residual pulmonary tissue. Particularly is this true in resectional therapy for tuberculosis of the lung where inevitably some tuberculosis remains in the residual pulmonary tissue which must be prevented from overexpansion. In this sense, surgeons have come to realize that the commonly recognized pulmonary functions of ventilation and gas exchange can be completely preserved only if the space-occupying function of the lung is also recognized. The use of antibiotics is an important adjunct to thoracic surgery, but equally so are measures to promote early, rapid and complete expansion of the remaining pulmonary tissue.

PREOPERATIVE EVALUATION AND CARE

Except for the acute traumatic emergencies the majority of patients with pulmonary disease requiring surgery can be assessed preoperatively, and optimally prepared for treatment. Inquiry is directed along the following avenues:

A careful history often discloses associated infections or disorders which bear directly upon the pulmonary problem. Anemia, defects in blood coagulation, lymphadenopathy, symptoms of primary neoplasia elsewhere in the body, avitaminosis and psychic preparation are to be considered. Cough habits, quantity and character of sputum, extent and duration of smoking habits, and orodental hygiene should be evaluated. Many of these can be improved preoperatively for a brief period to advantage. Smoking should be reduced, tracheobronchial irritation avoided, orodental hygiene improved, and upper respiratory and sinus infections controlled. Anemia, metabolic

deficiencies and avitaminosis can be effectively controlled with iron, transfusions, diet and vitamins.

Physical examination of the chest tends to be neglected with the ease of securing a chest radiograph, but much valuable information can still be heard in the chest which cannot be observed radiographically. Rales, bronchi, character of breathing, tracheobronchial secretions, etc., can be best evaluated by physical examination, which remains an important adjunct in the preoperative evaluation of surgical candidates.

The necessity and advantages of a preoperative x-ray of the chest are self-evident. Operative therapy cannot be planned without this essential adjunct, and often laminography and lipiodol instillation must be included if the proper operative procedure is to be employed.

Cardiac failure remains one of the prime causes of difficulty in the postoperative period and is the most common cause of mortality in the early postoperative period. Digitilization of the patient preoperatively has been used by many thoracic surgeons on an empiric basis, particularly if the history or physical examination suggests cardiac embarrassment is likely, and in recent years an increasing number of men have been satisfied with its value. Theoretic justification for preoperative digitalization on this basis is difficult, but practically its use has been gratifying.

Sputum culture is essential to proper antibiotic therapy preoperatively. Tuberculous patients require specific antibiotic therapy, and in the non-tuberculous patients not only the offending organisms but also their drug sensitivities should be determined for most effective preparation. The majority of respiratory tract pathogens are sensitive to penicillin, but any of the broad spectrum antibiotics may be used depending upon sensitivity studies. If antibiotic therapy is combined with postural drainage, even patients producing more than 30 cc. of sputum daily can be properly prepared for surgery within a few days.

In the tuberculous patient a minimum of 120 days of antibiotic therapy is employed. It is best to administer 1 gm. of a mixture of streptomycin and dihydrostreptomycin on an intermittent basis twice weekly, but combine it with 12 gm. of para-aminosalicylic acid daily (PAS). By this combined program bacterial resistance is reduced to a minimum. Recently isonicotinic acid hydrazid (INH) has been used in conjunction with the foregoing regimen in doses of 250 mg. daily.

Penicillin aerosol can be administered on an outpatient basis by employing a handbulb nebulizer. Penicillin, 50,000 units, is dissolved in 1 cc. of saline and administered four times a day. Local penicillin therapy, however, has no advantage over a systemically administered drug which actually diffuses through all the pulmonary structures.

Postural drainage remains an important adjunct to all preoperative preparation. Generally it is carried out by having the patient lie across the bed, hanging over the edge, with his head down and his hands and elbows supported on a low chair or stool. Five- to ten-minute periods four to six times a day are used, and it is especially valuable upon arising in the morning. It should also be practiced the morning of surgery prior to anesthetization. This regimen applies to lower lobe lesions since the upright position would be more effective in apical disease.

Occasionally there is a patient with extreme anorexia, depression or intractable fever from chronic pulmonary suppuration in whom cortisone can be used to advantage for a few days. The non-specific effects of the drug in improving appetite, reducing fever and inducing euphoria may improve the patient's preoperative status. Its use in this connection is not frequent and need not be encouraged.

There is no sounder basis on which to advise and practice thoracic surgery than a firm knowledge of respiratory function and its clinical evaluation. Unfortunately, however, there are no simple methods at the present time which are readily accomplished, fully understood or easily applicable to the problem case. It is quite simple with physiologic understanding to relieve a tension pneumothorax, control paradoxic motion of the thoracic cage or expand an atelectatic lobe by removing a bronchial obstruction, but it is difficult to predict whether a respiratory cripple will be produced by total right pneumonectomy in an elderly patient or whether resection or limited thoracoplasty will preserve more functions in certain tuberculous patients. This difficulty arises from the fact that respiratory function involves an evaluation of the mechanics of ventilation (the integrity and mobility of the thoracic cage and diaphragm, elasticity of the lung, pleural pressure changes, patent airway, etc.), intrapulmonary mixing of gases and respiratory dead

space, pulmonary gas exchange across the capillaries (diffusion, pressure gradients, membrane permeabilities, etc.), venous admixtures and shunts, and the pulmonary and general circulation. From a practical standpoint the ability of the patient to walk and exercise without respiratory distress, the vital capacity of the individual, the absence of cyanosis or signs of anoxemia and the nature of the lesion enable the surgeon to determine appropriate therapy without extensive measurements of the foregoing variables. The surgeon's goal is to preserve or improve the existing respiratory function, yet deal appropriately with the underlying lesion. Further derangements of respiratory function during the operative and postoperative period should be held to a minimum. An occasional case requires bronchospirometry and an entire battery of pulmonary function studies, but these are not routinely employed.

Patients with heavy secretions will have less difficulty with either the face-down (Overholt) or supine position. However, if the patient has been properly prepared with postural drainage and antibiotics, rarely will the secretions be too troublesome in the usual lateral position. Similarly, if the anesthesia is properly administered, the well-being of the patient is equally well served in any position; and the surgeon should use the position and approach which offers optimum facility in his task.

OPERATIVE MANAGEMENT

Anesthetic Agent. Pulmonary surgery demands close cooperation between the anesthesiologist and surgeon. This cooperation is best expressed by mutual discussion and decision as to the anesthetic agent or agents of choice in a particular case, respecting always the cardiorespiratory status of the patient. Ether, cyclopropane, nitrous oxide, curare, pentothal® and other agents have been successfully employed, with strong individual preferences. Each anesthetic agent has a special usefulness and variable drawbacks, and the surgeon must entrust the patient and himself to the skill of the anesthetist with a wide variety of agents. However, the anesthetist must realize that "the patient comes to the operating theatre for an operation, not an anesthetic." and cooperate accordingly.

Alveolar Ventilation. Of equal importance to the anesthetic agent is the method of administration. Initially it was believed that many of the respiratory complications of anesthesia were related to the position of the patient during the operation. However, it has been rather conclusively shown that the development of carbon dioxide retention and respiratory acidosis are related to inadequate alveolar ventilation rather than the open thorax or the patient's position on the operating table. With alteration in the rate and depth of respiration and change in the effective mid-position of the lung with an open pneumothorax there is a tendency for "dead space" ventilation to increase and for effective alveolar ventilation to diminish. It is the anesthetist's responsibility to insure adequate alveolar ventilation throughout the operation, and retention of carbon dioxide is of equal concern to the prevention of anoxemia. Both of these pathologic-physiologic alterations are related to respiratory acidosis, circulatory competence, and cardiac irregularities and arrest.

Endotracheal Intubation. The use of an endotracheal tube for proper anesthesia in thoracic surgery is imperative. Not only does this insure patency of the airway, prevent obstruction from laryngospasm, but also it provides the anesthetist with control over the respiratory mechanics during the period of the intrathoracic work. It also provides easy access to the tracheobronchial tree for catheter aspiration of secretions. In the adult, endotracheal intubation is completely rewarding and nonirritating; in children, endotracheal control is also essential but care must be exercised to avoid the slightest injury to the larynx or postoperative tracheal edema and obstruction might require tracheotomy. Before extubation, during and at the conclusion of the operative procedure, catheter aspiration of the tracheobronchial tree is accomplished. This permits the patient to leave the operating room without retained or pooled secretions; and if the patient is awake at the conclusion of the operation and in possession of his normal protective reflexes, postoperative retention of pulmonary secretions and atelectasis will be prevented.

Blood Loss and Shock. Replacement of blood loss and prevention of shock are important in thoracic surgery. The surgeon must be aware of the rather large volumes of blood lost in even the average thoracotomy. Weighing of the sponges or attention to the amount of blood aspirated into the suction bottle are clues as to the extent of blood loss. Measured blood loss

by several methods (Evans blue, weighing of the sponges, etc.) has shown that the average lobectomy patient loses 1,000 to 1,200 cc. of blood and the average patient undergoing segmental resection loses 1,500 to 1,600 cc. of blood. To insure adequate replacement a large bore (No. 15 to 18) needle should be inserted into an arm vein prior to surgery. In fact it is often safer to have two indwelling needles in the arm early in the operation. A saphenous vein cut-down placed just above the internal malleolus is especially useful in infants and small children. In adults, however, the arm veins are preferred to avoid postoperative thrombophlebitis. Ordinarily little or no salt is lost during surgery; and since salt retention to varying degrees follows surgery, the additional fluid administered should be dextrose in water.

Expansion of Remaining Lung and Adjustments of Intrapleural Pressures. Prior to terminating the operative procedure the residual pulmonary tissue is completely expanded by gentle positive pressure through the intratracheal tube, and air is aspirated from the pleural space by a large bore needle or through an intercostal catheter. The motion of both sides of the chest is observed and auscultation confirms the exchange of air into remaining pulmonary tissue. Refined adjustments of pleural pressures with manometer measurements are rarely necessary. When a large quantity of effusion is expected or when a persistent air leak is anticipated, one or two large intercostal tube drains are connected to an underwater seal or suction device. The aim is rapid and complete expansion of the remaining pulmonary tissue.

Bronchoscopy. Bronchoscopy at the end of the operative procedure is rarely necessary, for secretions can be cleared through the endotracheal tube prior to extubation. However, if the catheter fails to clear the tracheobronchial tree completely or if there is suspicion of retained tracheobronchial secretions with atelectasis, there should be no hesitation in employing bronchoscopy after extubation.

POSTOPERATIVE CARE

After a *lobectomy or segmental resection* emphasis is properly placed upon early and complete expansion of the remaining pulmonary tissue. This militates against infection in the residual pleural space and also enables maximal preservation of pulmonary function. To accomplish rapid re-expansion of the residual pulmonary tissue one or two large intercostal tubes are placed and brought out through a stab wound separate from the main incision. Some surgeons prefer Foley catheters, others straight Robinson catheters of large bore, and still others large bore right-angle tubes. These intercostal drainage catheters can be connected to a simple underwater seal directly, or a trap bottle may be interposed between the catheter and underwater seal to collect fluid or blood. A three-bottle catheter suction drainage consisting of first the trap bottle, then a second water-seal bottle, and finally a valve bottle to which the suction is applied in a controllable fashion is preferred by many surgeons. The negative pressure delivered to the system is regulated by a glass tube connected to the atmosphere on one end and submerged below the water level on the other. Eight to 10 cm. of submersion of the tube afford 8 to 10 cm. of negative pressure intrapleurally. Care must be taken to preserve the patency of the intercostal tubes by frequent observation, "milking" of the tube to free fibrin or blood clots, and occasionally by irrigation with an antibiotic solution. The tubes generally fail to function after a few days. They may be removed if the lung is completely reexpanded without air leak or if the fluid drainage is less than 50 to 75 cc. per day. X-rays of the chest combined with physical examination should confirm complete expansion of the lobe with minimal fluid in the pleural space prior to removal of the tubes. Occasionally in segmental resection air leaks persist for several days and a tension pneumothorax would result if the tube were prematurely removed. One must be particularly alert to this possibility after any tube has been removed, or if a thoracotomy has been closed without intercostal tube drainage.

The *postpneumonectomy case* offers different problems. The pleural space is not drained ordinarily, but at the end of the operation the intrapleural pressure is adjusted to about minus 8 to 10 cm. of water. This pressure is raised postoperatively by the accumulation of fluid in the pleural space; and if respiratory embarrassment appears or mediastinal shift is apparent, a needle should be inserted anteriorly in the second or third interspace and readjustment of intrapleural pressure accomplished.

Contrariwise if heavy coughing should result in marked subcutaneous emphysema, excessive negative intrapleural pressure might result with respiratory embarrassment from herniation of the mediastinum into the operated side. Pleural pressure would again have to be adjusted. Rarely does a bronchial fistula occur postoperatively, but this, too, would require relief of a tension pneumothorax in the postoperative period.

X-rays are extremely valuable in the postoperative period to follow and direct the management of the pleural space after thoracotomy.

If the anesthetist has cleared the tracheobronchial tree adequately at the conclusion of the operative procedure and if the patient is sufficiently awake that he possesses his pulmonary reflexes, little difficulty should be encountered in maintaining the tracheobronchial tree free of secretions. The patient should be turned frequently, encouraged to take deep breaths and to cough, and excessive opiates with attendant respiratory depression should be avoided. Atelectasis, pneumonitis and pulmonary edema are thereby preventable postoperative complications.

When excessive thoracic pain handicaps the effective clearing of the tracheobronchial tree by cough, intercostal nerve block may prove quite useful and successful in enabling the patient to improve his effective cough. Several nerves must be blocked and one of the longer lasting anesthetic agents may be used. Caution must be observed not to deposit the novocain too close to the spine, for seepage of the anesthetic agent into the cord has been reported.

Endotracheal catheter aspiration is both simple and valuable in aiding the patient to clear tracheobronchial secretions effectively. A No. 16 or L8 French catheter is passed through the nose with the patient sitting or propped up. The tongue is grasped and pulled forward, uncovering from the epiglottis some of the glottic opening. The patient is asked to take several deep breaths, and on inspiration the catheter is rapidly advanced into the trachea. Suction is applied and the trachea and major bronchi cleared. The suction must be interrupted every few seconds to permit breathing. Ordinarily this procedure requires no anesthetization; but if an unduly sensitive gag reflex is present, 1 per cent pontocaine® can be sprayed into the back of the throat. This procedure can be repeated very frequently if necessary, and much of its virtue lies in the effective cough it stimulates.

Bronchoscopy is rarely necessary in the postoperative course if the previously described measures have been practiced. However, if the simpler measures fail to provide a clear and adequate tracheobronchial tree, there should be no hesitation in using the bronchoscope to this purpose postoperatively.

Tracheotomy is occasionally indicated in the postoperative period if frequent aspiration of the trachea is required to preserve a clear tracheobronchial tree and if this is difficult by catheter aspiration. In children and much less commonly in the adult, significant postintubation laryngeal edema may occur and a tracheotomy is wisely utilized to advantage. Beneficial effects have been striking in selected cases of crushing injuries to the chest and after extensive thoracoplasties.

Prevention of infection in the pleural space is generally begun preoperatively with the administration of penicillin and streptomycin in the twenty-four-hour period prior to operation. At the conclusion of the operation if contaminated material has been spilled during surgery, a mixture of 500,000 units of penicillin and 1 gm. of streptomycin may be dissolved in a few cubic centimeters of saline and instilled into the pleural space. Postoperatively penicillin and streptomycin are administered for two to five days, depending upon the rapidity of lung re-expansion or the necessity of pleural aspiration to relieve fluid or air accumulation. Wide spectrum antibiotics are used; but if organisms can be recovered by culture or smear, sensitivity studies can be done and the appropriate antibiotic agent employed. Antibiotic agents are valuable adjuncts in the prevention of infection but must not in any sense replace sound surgical principles.

Oxygen is employed almost routinely in the postoperative period and may be administered by nasal catheter or by oxygen tent. If a nasal catheter is employed, care must be taken that oxygen is connected to it and not to any other indwelling tube, a mistake which has been made all too frequently. Ordinarily, oxygen is necessary for only twenty-four to forty-eight hours, and its use may be discontinued when the pulse rate drops below 100 or the patient's condition obviously no longer requires it.

Even though the operative blood loss is re-

placed during or shortly after the completion of the operative procedure, there is often a continued seepage of blood into the operative wound and into the pleural space. The administration of blood in the postoperative period to match this loss is desirable. It ranges from 500 to 2,000 cc.

There is considerable danger in the postoperative period of pulmonary edema and heart failure. In fact, these are the most frequent causes of death after pulmonary resection, particularly in the elderly patient. The usual uncomplicated pulmonary resectional case requires little or no intravenous fluid postoperatively. The fluid intake need not exceed 2,000 cc. daily in the average case, and this quantity may generally be taken by mouth. There is a natural tendency for salt retention following any surgical procedure; and if fluid need be administered intravenously, 5 to 10 per cent dextrose in water is preferable to saline.

Hypotension in the immediate postsurgical period may require intravenous supportive therapy, but blood and nor-epinephrine should be used rather than excessive amounts of water or salt.

Abnormal losses of fluid and electrolytes are uncommon in pulmonary operations; but if they should occur, these abnormal losses should be included in the calculations of the daily needs of the patient.

Breathing and postural exercises initiated early and employed vigorously in the postoperative period are highly valuable. They favor re-expansion of the lung, improve ventilation, restore normal muscle strength and posture, and prevent thoracic scoliosis. Early ambulation is part of the postoperative rehabilitation program.

With the employment of these preoperative, operative and postoperative measures, safe conduct of the patient through major and difficult thoracic surgical procedures is best insured.

Complications Following Pulmonary Surgery

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Improvements in the over-all results obtained in thoracic surgery during the years following World War II are to be regarded as one of the most significant milestones in the history of medicine. It is recognized by all observers in this field that such progress was made possible by advances in numerous fields, including a more accurate diagnosis, better preoperative care, improved surgical technic, anesthesia, prevention and treatment of shock, and in better over-all postoperative care. Reduction of the morbidity and mortality rates in patients undergoing chest surgery has resulted to a large extent from better understanding of the physiologic status of these patients in the immediate postoperative period. Cardiorespiratory function tests prior to operation give the surgeon important information which, coupled with the clinical impression of the general state of health of the patient, makes him aware of what to expect in the postoperative period. Measures to foresee and prevent complications are now routine in everyday practice and have contributed greatly to the relative safety of modern thoracic surgery. An understanding of the cause and effect relationship of late complications of resectional surgery has also helped to reduce the incidence of these undesirable developments, the more serious and dreaded of which are bronchopleural fistula and empyema. It has not been long since the seriousness of these complications as well as the frequency with which they occurred were an absolute deterrent to physicians, internists and surgeons alike, in advising pulmonary resection to patients who needed it. This discussion is confined to the complications occurring after pulmonary surgery alone and will not extend into the realm of thoracic surgery in general. More specifically, it will concern itself with those complications arising as a result of resectional surgery in one form or another which constitute by far the large majority of operations on the lung.

When a patient undergoes pulmonary surgery, his system is exposed to an interplay of influences, the proper and favorable outcome of which is of the utmost importance. The so-called critical period in the postoperative course is rather an ill defined one and varies from one patient to another. Thoracic surgeons are all too familiar with instances where an adjustment to normalcy is made with amazing speed, whereas others who have undergone less serious surgical measures are confronted by a critical and prolonged fight to keep the balance from tipping over to a gradual or sudden downhill course. The exact reason for such differences probably is a composite of factors, some of which are poorly understood. An attempt will be made here to divide them into individual factors, bearing in mind that in any single case various combinations of these together with other ill defined factors probably are in progress. Consideration will be given first to the immediate postoperative period which usually covers the hospital stay of the patient.

Hemorrhage. Careful, meticulous control of hemorrhage is one of the principles of all surgery. It is perhaps more important in thoracic surgery than elsewhere. The total blood loss should be calculated during every thoracic operation. Only by this means can the patient receive the proper amount of blood during surgery. After the operation has been completed and the patient has been returned to his bed, there is always a certain amount of bleeding into the pleural cavity. If the surgeon has been cautious, bleeding will be minimal, although sometimes more profuse bleeding cannot be prevented in spite of careful hemostasis because of persistent oozing from large denuded pleural surfaces or from some change in the blood-clotting mechanism. The patient who shows signs of bleeding in the postoperative period must have careful and close attention. Accurate blood replacement by transfusion is essential in order to avoid the disastrous effects of a low hemoglobin level and

the subsequent lowered oxygen-carrying capacity of the blood. Such a situation, even if left uncorrected for a short period of time, can lead to cardiocirculatory failure which in most instances is irreversible.

The presence of postoperative bleeding can be determined readily if frequent hemoglobin and/or hematocrit determinations are made. Such determinations should be done at the completion of the operation and repeated every hour until the patient has reached a stable condition. Thereafter, the determinations are made at increasingly longer intervals, with perhaps three such readings on the day after surgery for partial lung resection and the determinations continued for three days after pneumonectomy. A falling hemoglobin level, with a normal blood pressure and a patient in obviously satisfactory condition, signifies the restoration of blood volume and is a welcome sign. However, a falling hemoglobin with low blood pressure and signs of peripheral failure is a certain sign of hemorrhage, and the patient must receive whole blood transfusions if his life is to be saved. A rising hemoglobin signifies hemoconcentration and impending shock not on a hemorrhagic basis. In such circumstances the patient requires fluids, especially plasma or blood. When the chest is drained, close observation of the amount of drainage is important and will sometimes indicate the amount of bleeding. However, the amount of drainage is a satisfactory index only when the system is functioning adequately. Reoperation for bleeding in the postoperative period is rarely indicated and should be avoided by careful hemostasis at the original operation and by adequate replacement in the postoperative period should bleeding occur. However, if there is postoperative bleeding and a clot forms in the pleural cavity sufficient in size to shift the mediastinum, reoperation may be imperative since the mechanical factor of lung and mediastinal compression must be removed.

Air Leaks. Except when the entire lung is excised, patients having undergone surgery of the lung may have air leaks of varying magnitudes and duration. This is understandable in spite of the most meticulous attempts to prevent air leaks since it is technically impossible to obliterate completely minute bronchiolar and alveolar leaks. In order to permit the free exit of air from the pleural cavity, the pleural cavity is drained and routinely the intrapleural tube is connected to an underwater sealed bottle at the time the chest is being closed. Only one intrapleural drainage tube is employed because there appears to be no benefit from more than one. Suction is applied to the intrapleural tube when the patient is returned to his bed. A negative pressure of approximately 2 cm. Hg is applied to the drainage system. In order to prevent a build-up of positive pressure in the pleural cavity resulting from mechanical failure in the drainage suction system, a pop valve or safety mechanism is included in the latter. It is a mercury manometer set to prevent more than 1 mm. Hg positive pressure. This mechanism allows the escape of larger quantities of air during cough and movement. Large volumes cannot be removed quickly by a suction drainage system of small suction volume per unit time. In an effort to keep the chest tube open it is milked and/or agitated frequently. The sudden stoppage of air leaks is carefully checked to ascertain the possibility of faulty drainage and collapse of the lung.

It is believed that a No. 30 or 32 French catheter or tube is desirable for drainage of the pleural cavity in the adult. This tube should have multiple holes cut in its side and the tube should be extended from diaphragm to apex and anchored by a loose suture sling of catgut to the lateral aspect of the pleural cavity. If the tube is allowed to fall posteriorly, it can be sealed off from the general pleural cavity by the lung, even though it is unexpanded. The larger the size of the intrapleural and other tubes of the drainage system, the less the likelihood of serum or blood clotting within the system and occlusion of the tube. Milking or agitating the tubing aids in preventing the clotting of serum or blood in the tubes. Normally, air leaks continue for a few hours to a few days. It is important to differentiate between such leaks and those that occur later in the postoperative course, ranging from a week to several months postoperatively. The former are referred to as broncho-alveolopleural leaks or fistulas, whereas the latter are usually bronchopleural and represent direct communication between a former surgically divided and closed bronchus and the pleural cavity. It is usually advisable to wait for an average period of forty-eight hours following complete cessation of air leaks before the intrapleural tube is removed. When this tube

is removed, a formerly placed suture is tightened to close the skin opening. A safe, working method of controlling persistent postoperative leaks is carried out by the use of a gradually increasing negative pressure, on occasion as much as 5 cm. Hg. Unless a major bronchus is open, this method invariably pulls the remaining lung to the chest wall and seals the tiny openings in the parenchyma. Occasionally broncho-alveolo-pleural leaks develop after the tube is removed but these can be controlled easily by closed tube drainage; if minimal, nothing is done.

It is well to point out that chest wall or subcutaneous emphysema, particularly of increasing amount in a patient having undergone excisional surgery with or without a tube for intrapleural drainage, is a sign of tension developing within the pleural cavity. Prompt attention should be given to relief of the intrapleural tension even though a suction drainage system seemingly is working adequately. The tissue emphysema is of no importance except that it is a sign of and indicates the presence of air under tension in the pleural cavity.

Air leak in the immediate postoperative period following pneumonectomy is not anticipated, and if found it is a definite indication of improper closure of the bronchial stump. The same condition may account for the sudden complete rupture of the bronchial stump. This is a most serious complication and one that requires emergency treatment. It is usually a ball valve type of leak which creates increased intrapleural pressure with a shift of the mediastinum. Immediate closed thoracotomy or, in the absence of a proper sterile set-up, needle aspiration can be life-saving. The authors have had no experience with this complication in their patients and have not attempted a primary reclosure of the bronchial stump by open operation. Of eleven thoracic surgeons who were recently questioned, only three had attempted such closures.[1]

Atelectasis. Pulmonary atelectasis has been and continues to be a common complication in the early postoperative period. Investigators have labored relentlessly to determine its cause and work out a plan for its prevention. Seybold[2] in his study ascribed a decreased ventilatory capacity as a major cause of such collapse. As contributing factors he cited trauma to the muscles of respiration, pain in the operative area, injury to the phrenic nerve, excessive bronchial secretions and the occasional presence of a bronchopleural fistula. In an effort to reduce trauma to the chest wall musculature to a minimum, the authors use a wide low sweep on the posterior aspect of the conventional posterolateral incision. It is believed that this prevents interruption of the nerve supply to a much greater portion of the muscles than in the standard incision. Temporary or permanent injury or deliberate paralysis of the phrenic nerve should be avoided in pulmonary resections in order to prevent atelectasis and/or impairment of pulmonary function. Injury to the intercostal nerves immediately adjacent to the intercostal incision can hardly be prevented; however, the injection of procaine into these nerves before spreading the ribs can prevent possible ill effects in a patient who is being maintained in a light plane of anesthesia, as in cardiac cases. Deaton and Bradshaw,[3] in commenting on the control of postoperative pain in the immediate period of recovery with the use of efocaine injected into the intercostal nerve, reported satisfactory results in sixty-five of eighty-four cases. The sixty-five patients required much less sedation, about 60 per cent of the amount used in non-treated cases. No untoward reactions were noted. Injections were made with the chest open. The authors have had an unsatisfactory experience with such measures. Pain is controlled with the judicious use of sedatives, but the cough reflex is not depressed appreciably. This control is enough to allow sufficient ventilation and expulsive efforts of coughing.

The nature and quantity of the tracheobronchial secretions are of the utmost importance in the pathogenesis of atelectatic pneumonia. Devices to liquefy secretions, such as croup tents, expectorants and aerosol medications, are used when indicated. Intratracheal catheter aspiration and its technic are by now well known and used freely. When carefully done the latter can be as effective as a bronchoscopic aspiration in accomplishing a satisfactory tracheobronchial toilet. Bronchoscopic aspiration is used freely when indicated. For a postoperative patient with a "wet" lung and much tracheobronchial secretions a non-obstructive tracheotomy should be done. It may be life-saving in many instances. Non-obstructive tracheotomy is especially helpful in instances where excursions of the chest wall have been seriously impaired as a result of the opera-

tion or injury, or in an uncooperative patient, especially when the patient is physically or mentally unable to cooperate. However, it is imperative to avoid non-obstructive tracheotomy when there is left heart failure and pulmonary edema. When a diagnosis of atelectasis has been made, it is important to begin treatment immediately. Simple measures are initiated, but if unsuccessful within a few hours the more radical methods of combating atelectasis are used. First, the patient is instructed to move, turn and cough more frequently. The carbon dioxide inhalation therapy is used more often. When this fails, tracheal aspiration is tried. If satisfactory results are not obtained, bronchoscopic aspiration is resorted to. Finally non-obstructive tracheotomy is employed if repeated bronchoscopic aspirations seem to be needed. More often than not, the bronchoscopist is unable to find definite mucous plugs obstructing that portion of the lung but reports diffuse erythema with hemorrhagic secretions distributed over the entire bronchial tree. It is important to avoid too much sedation before bronchoscopy since it is desirable for the patient to retain a good strong cough reflex and be able to move about freely after bronchoscopy.

Cardiac Failure. One of the complications of pulmonary surgery in the immediate postoperative period is cardiac failure. In some patients the cardiac difficulty is related to a known impairment of the heart before operation. However, in most of the patients affected this occurs even though previous evidence of heart disease could not be determined. It is obvious that the frequency of difficulty from cardiac failure and/or coronary heart disease is related to the age of the patient and the amount of lung tissue removed. In a recent survey of thirty deaths following pneumonectomy for cancer of the lung, these patients for the most part being in the older age group, nine died as a result of cardiac failure and five from coronary occlusion. The authors have also been impressed recently by the relative frequency of acute coronary occlusion with or without myocardial infarcts in these patients. Surgeons should be constantly on the alert in the first few days following surgery for any unusual degree or location of chest pain. It is a simple matter to ascribe all chest pain in the post-thoracotomy patient to the surgical wound, thus overlooking a much more important and often fatal complication in the heart. In combating this serious complication there appears to be no assured successful treatment. A careful survey of the heart before operation is always recommended. Digitalization is indicated before operation if there is impending cardiac failure. Every precaution is taken to prevent shock during and immediately after operation. The prevention of infection is most important because a period of high fever in a pneumonectomy patient is often accompanied by shock or peripheral failure and then central cardiac failure. Since a large amount of lung tissue is removed by pneumonectomy, these patients should be kept in an oxygen tent or given oxygen therapy for several days. They should be kept at bed rest longer than other patients after operation and should be rapidly digitalized at the first sign of cardiac irregularity, pulmonary edema or engorgement of the liver.

Empyema and Bronchopleural Fistula. Pleural empyema with or without bronchopleural fistula may occur early or late in the postoperative period. The importance given to these complications by surgeons is well warranted since both conditions are serious and incapacitating to the patient, even though they do not usually result in fatalities. In a previous paper on this subject[1] the authors made a clear differentiation between those cases occurring in patients who have undergone pneumonectomy on the one hand and those having resections involving less than the entire lung. The necessity for this distinction becomes obvious if one considers the protective influence of any portion of an expandable lung remaining in the pleural cavity. The obliteration of any dead space is of primary importance in avoiding the persistence of infection in a cavity. A nonspecific protective barrier is established when pleural surfaces are approximated and antibodies and antibiotic agents are allowed to exert a direct influence over microorganisms.[4] It is generally agreed by most thoracic surgeons that their figures are much higher for such complications following total pneumonectomy than those following less extensive resections. Overholt[5] in 1946 reported an incidence of bronchopleural fistula in 2.9 per cent and of empyema in 7.2 per cent of pneumonectomies in tuberculous patients between the years 1944 to 1946. Shaw and Paulson[6] discussed an incidence of empyema of 21.3 per cent in lung abscesses. Zelman[7] found 15.2 per cent bronchopleu-

TABLE I

COMPLICATIONS FOLLOWING PULMONARY SURGERY

1941–1953 Late Complications	Carcinoma			Tuberculosis			Lung Abscess			Bronchiectasis		
	Pneumonectomies	Lobectomies	Segmental Resections	Pneumonectomies	Lobectomies	Segmental Resections	Pneumonectomies	Lobectomies	Segmental Resections	Pneumonectomies	Lobectomies	Segmental Resection
Total No.	111	3	0	23	26	14	2	15	1	12	46	22
Total No. of Empyemas	4	0	0	2	0	0	0	5	0	1	1	0
Total No. of Empyemas without Bronchopleural Fistula	2	0	0	1	0	0	0	1	0	1	0	0
Total No. of Bronchopleural Fistulas	2	0	0	1	2*	2*	0	4	0	0	1	0
Hospital Mortality	29	1	0	3	1	0	0	1	0	1	1	1

* Broncho-alveolo-pleural fistulas—noted in text.

ral fistula and 3.8 per cent empyema in tuberculosis.

The authors[1] reported complications following pneumonectomy for the period 1941 to 1952. During this time bronchopleural fistula occurred in 2.16 per cent and empyema without bronchopleural fistula occurred in 5.4 per cent. The group comprised 185 consecutive pneumonectomies for all kinds of pulmonary disease. Table 1 is a summary of the complications in 275 consecutive resections of all types in private patients between the years 1941 to 1953 inclusive. It is to be noted that the incidence of bronchopleural fistula was higher in the group of lobectomies for lung abscess, four of fifteen, or 26.6 per cent. However, these occurred in the years 1942 and 1943, the last one in 1946. Next comes the incidence in pneumonectomies for tuberculosis, one in twenty-three or 4.3 per cent, and this occurred in 1946 without the aid of streptomycin. The rate in pneumonectomies for carcinoma of the lung was two in 111 cases, or 1.8 per cent. The over-all incidence of fistula was eight in 275 resections, or 2.9 per cent. There were two patients with lobectomies for tuberculosis and two with segmental resection for the same disease in whom air leaks developed after the removal of the tube in the immediate postoperative period, none of which required closed thoracotomy or catheter suction. One needed a single aspiration. By conservative management the leaks were stopped and the lungs re-expanded in the remaining three patients. Distinction must be made between minor air leaks in the immediate postoperative period and a true bronchopleural fistula. The majority of the former are parenchymal leaks and can be referred to as broncho-alveolo-pleural fistulas. They are seldom troublesome and respond extremely well to conservative treatment. Some cases need closed thoracotomy with catheter suction for a few days. This minor maneuver usually suffices to control and stop the leak. True bronchopleural fistulas are usually derived from the larger bronchi—main, lobar or segmental—and are much more difficult to control. They are invariably followed by empyema, whereas the broncho-alveolo-pleural fistulas rarely if ever result in an infected pleural cavity. This is probably explained by the relatively sterile condition prevailing in the terminal bronchiolar and alveolar systems.

The reasons for the development of empyema

and bronchopleural fistula and their pathogenesis have received wide attention by many authors. In the case of bronchopleural fistula the presence of active disease at the site of division of the bronchus is a potent cause. The virulence of the infecting organism is important in lung abscess or in tuberculosis. There is no general agreement as to the effect of the type of bronchial closure used. It is generally accepted that non-absorbable sutures give the best results. The authors leave the crushed end of the bronchus and suture over this end after inserting one or two layers of mattress sutures proximally. Satisfactory results also are obtained by the widely used method of cutting proximal to the clamp and suturing the cut end of the bronchus with a single layer of fine silk sutures. In this series without exception the stump has been covered with some form of living tissue, often a pleural flap. After pneumonectomy when no other tissue is available for covering the bronchial stump, the esophageal wall can be employed with advantage to cover the stump. The esophagus has been used many times in this manner and the outcome has been highly satisfactory. No untoward results have occurred. It is of the utmost importance to cover the bronchial stump with living tissue although recently some surgeons have given up this step as a useless procedure. Brewer[8] has shown rather conclusively the importance of covering the bronchial stump in this manner.

The presence of a fistula is suspected when the patient has empyema, expectorates bloody fluid or develops a gradually increasing amount of subcutaneous emphysema. Its definite proof lies in the expectoration of a dye injected intrapleurally or by failure to maintain a negative intrapleural pressure on aspiration. When a bronchopleural fistula has developed, a definite plan of management should be undertaken. A sharp distinction must be drawn between a bronchopleural fistula after partial lung resection and a bronchopleural fistula after total pneumonectomy. Whether or not postoperative intrapleural tube drainage was carried out will definitely influence the course of the complication.

In a bronchial breakdown after pneumonectomy without tube drainage, if the air leak is large, a closed type of pleural drainage promptly instituted will prove life-saving. Where the leak of air from the bronchus is slow it would be more advisable to resort to a closed type of drainage as the first method of treatment, and this should always be done before open thoracotomy is used. After closed drainage has been instituted, it is important to instill an antiseptic solution or an antibiotic agent that is best suited for the bacteria found. It is also necessary to use an agent that will tend to seal over the air leak and not cause further breakdown of the bronchial stump by producing increased irritation or inflammation. It is believed that the best results are obtained by the use of sodium tetradecyl sulfate 1:500 and azochloramid 1:3300 with sulfanilamide since it is a good non-specific antiseptic agent, a mild detergent and apparently aids the quick sealing of air leaks. When desired or when indicated, a specific antibiotic agent may be added. If the air leak can be overcome and the infection prevented or eliminated, the tube may be removed. Should this conservative management prove unsuccessful, open thoracotomy must be used. It is best to select a type that will remain open permanently. Open thoracotomy should be continued for approximately six months. Eventually it will be possible to permit retraction of the mediastinum into the empty pleural space. The more the mediastinum retracts into the empty pleural cavity, the easier will be its obliteration by thoracoplasty. It is often an advantage to add a phrenic avulsion to the management of the infected space since elevation of the diaphragm aids in obliteration of the pleural cavity. After the pleural cavity has been reduced in volume as far as possible by this method, multiple stage thoracoplasty may be necessary to obliterate the remaining space finally. This will cure the empyema and close the bronchopleural fistula. Primary closure of the bronchopleural fistula after pneumonectomy has not been undertaken by the authors and probably is unwise. By following the foregoing plan all bronchopleural fistulas occurring after pneumonectomy have been finally and completely cured except where the patient died from his disease before treatment could be completed; however, it is a long and difficult plan of treatment, especially for the patient.

When the entire lung has not been removed, the problem of bronchopleural fistula is entirely different and definitely more amenable to treatment. One must distinguish between bronchopleural and broncho-alveolo-pleural fistulas,

since the latter usually occur while the initial drainage tube is in place and the air leak is overcome before the initial tube is removed. Where it is truly a bronchopleural fistula, an opening in the amputated bronchial stump, several methods of treatment are available. A closed thoracotomy with irrigation and suction as described under pneumonectomy often is successful. The fistula and resulting empyema frequently can be remedied by a single stage thoracoplasty. It is also possible to resort to exploratory thoracotomy where the remaining lung is freed up and a decortication done. Additional lung tissue can be resected along with the bronchopleural fistula. Murphy[11] and others concurred with this view. A simultaneous thoracoplasty is carried out if necessary to permit the remaining lung tissue to fill the pleural space. If the last remaining lobe is thus resected, the residual pleural space can be treated as described for a contaminated pleural space after pneumonectomy. The chest is closed without drainage and infection may thus be avoided. Five patients developed a bronchopleural fistula after lobectomy. One required thoracoplasty to effect a cure and another was treated by transplanting a pedicle muscle flap into the bronchus and the small remaining pleural space. The others closed and were healed completely by conservative management.

The etiology of empyema, of course, is bacterial. The latter can be traced from any source but most commonly are derived from the lung parenchyma, the bronchus, lymphatic vessels, the pleural membranes or the chest wall. Exogenous infection from surgical intervention is rarely the cause of empyema. The problems of empyema following pneumonectomy are different from those noted after less extensive pulmonary resections. It is imperative that every possible step be taken to prevent empyema. Extrapleural dissections to remove all adherent pleura are urged to prevent inadvertent opening of diseased tissue and insure the removal of all diseased pleura. Care is taken to avoid gross spillage into the pleural cavity from the bronchus. The authors use a closed technic of closure although a careful open procedure may give equally safe results. Where there is contamination of the pleural cavity during pneumonectomy the authors have been using a combination of sulfanilamide, azochloramid 1:3300 in sodium tetradecyl sulfate 1:500.[9,10] This material is placed in the pleural cavity at the completion of the operation and the cavity is closed without drainage. The pleural cavity is aspirated and the same mixture instilled each day for three days after operation or until three negative pleural cultures are obtained. In twenty-nine consecutive patients who had a grossly contaminated pleural space at the time of pneumonectomy all escaped infection or empyema except one. This patient could not have antibiotic therapy because of allergic reactions. The others received prophylactic antibiotic agents as indicated after surgery.

Pleural empyema without bronchopleural fistula occurred in the present series of patients about as often as with bronchopleural fistula. The frequency was essentially the same in the last series reported by the authors.[1] Empyema almost always accompanies a true bronchopleural fistula but rarely follows a bronchoalveolo-pleural leak. In one patient the sequence of events undoubtedly was empyema at first and then bronchopleural fistula. This was the circumstance in the bronchopleural fistula that occurred in the patient with tuberculosis. In another patient empyema developed as a result of a small superficial wound that ulcerated into the pleural cavity. The management of a definite case of empyema resolves itself into one of several forms of treatment or frequently a combination of several.

Sterilization of the pleural cavity by aspiration and instillation of an antiseptic and/or antibiotic agent is probably the simplest method of treatment. It has been found here that a mixture of azochloramid 1:3300 in sodium tetradecyl sulfate 1:500 with sulfanilamide crystals is most effective.[12] The aspiration and instillation are continued daily until negative smears and cultures are obtained. The patient should also be given an appropriate antibiotic agent. The bacteria least likely to be eliminated by this method are hemolytic staphylococcus aureus or albus. When aureomycin was added to the mixture, it has on at least two occasions eliminated this organism. If this method fails, thoracotomy, either open or closed, should be instituted to provide adequate drainage. This may be sufficient in many instances to control the infection in patients who have had only a lobe or segments removed, especially when the remaining lung tissue can expand enough to obliterate

the pleural space. The lobectomy patient with empyema who has had a closed thoracotomy may receive the irrigations prescribed for pneumonectomy with bronchopleural fistula. However, if bronchopleural fistula is not present, streptokinase and streptodornase can be added with great benefit. Kent[13] reported six cases of empyema without fistula which responded satisfactorily to this method. Thirteen others who had fistula, too, received tube drainage and antiseptic instillations. Eleven of these were cured, one required a thoracoplasty and one had a recurrence. The patient with empyema after lobectomy who is not cured by needle aspiration and sterilization or by tube drainage with irrigation and sterilization may have the empyema space collapsed by thoracoplasty, or on rare occasions may require decortication with or without simultaneous thoracoplasty.

A patient with empyema after pneumonectomy presents a more serious problem than the patient with empyema after partial lung resection and a greater effort should be made to cure the empyema without surgery. If a cure is not accomplished by needle aspiration and sterilization or by administration of an appropriate antiseptic or antibiotic agent, closed tube drainage with a strict routine should be instituted. The infecting bacteria must be identified and the sensitivity of the infecting organism to various antibiotic agents determined. After an intrapleural drainage tube is inserted, the pleural cavity should be instilled through the tube once every day with one ampul of streptokinase and streptodornase in 20 cc. of distilled water to which is added an appropriate antibiotic agent in sufficient quantity. This same antibiotic agent should be given systematically by mouth or injection, as the case may require. After the streptokinase, streptodornase and the antibiotic agent have been placed in the pleural cavity, the intrapleural tube is occluded for four hours, after which the clamp is removed and drainage allowed by underwater seal mechanism for four hours. Afrer this eight-hour period the pleural cavity is irrigated every four hours with sodium tetradecyl sulfate 1:500 in azochloramid 1:3300 to which has been added sulfanilamide. The whole treatment must be carried out under rigid aseptic conditions. When three successive intrapleural fluid cultures are found to be negative for bacteria, the intrapleural tube is removed and the tube opening closed by a single suture. The pleural cavity is aspirated by needle and instilled with sodium tetradecyl sulfate, azochloramide and the appropriate antibiotic agent for three successive days and intrapleural cultures again obtained. If the cultures prove to be negative, the empyema will be overcome or cured. One may by the trial and error method use other antibiotic agents. If the treatment is to be successful, it will not require more than a week or ten days. Long-continued unsuccessful treatment is to be avoided. If this method fails, it will be necessary to perform an open thoracotomy followed in approximately six months by multiple stage thoracoplasty, as described under bronchopleural fistula after pneumonectomy.

Postoperative Chest Wall Pain. Late and long-continued thoracic pain after pulmonary resection or, as a matter of fact, after major open thoracotomy for any thoracic operation occurs rarely. However, when it does persist, it proves rather distressing to the patient and may be incapacitating. It is thought to be traumatic intercostal neuritis when the pain is located on the chest wall. The oppressive pain that the patient cannot locate or the examiner cannot find is likely to be neuritis of the phrenic nerve. Two of the patients with traumatic intercostal neuritis have been relieved by resecting the transverse process and avulsing from the spinal cord the involved intercostal nerve roots, usually two in number. One patient who was thought to have neuritis of the phrenic nerve after pneumonectomy was relieved by avulsion of the phrenic nerve. It is believed that the one patient not completely relieved by avulsion of the intercostal nerve roots might have been relieved if he had permitted resection of the phrenic nerve. This nerve should not be removed for relief of pain except after a pneumonectomy. The authors have not felt the need for phrenic nerve avulsion for the relief of pain except after pneumonectomy.

CONCLUSION

This manuscript has dealt with the problems besetting a surgeon in the postoperative care of patients who have undergone pulmonary surgery. The problems do not necessarily follow a single pattern and many times tax the

ingenuity of the surgeon and his surgical knowledge. A careful balancing of the physiologic responses of the patient against the disturbances caused by the surgical intervention is many times a precarious battle involving the control of hemorrhage, the proper expansion of the remaining lung with stoppage of air leaks, and maintenance of clear air passages and adequate ventilatory capacity of the thorax. Unfortunately, in spite of detailed attention to these factors many patients succumb to major surgical procedures carried out on the lung from a combination of cardiac and/or pulmonary insufficiency for which little, if anything, can be done. The only solace to the surgeon lies in his having correctly evaluated these patients and having expected such results. It is only proper that the latter type of patients should be eliminated from the surgical lists as far as possible, provided they suffer from benign disease with little incapacitation. Obviously, many such risks must be taken when the patient suffers from a malignant disease.

The late complications, namely, bronchopleural fistulas and empyemas, are a continuous challenge to surgeons, especially in the field of their prophylaxis. It is believed that this challenge can be met by meticulous attention to careful surgical technic and early proper therapy if contamination has inadvertently taken place. The already decreased incidence of these complications compared to that of a decade ago speaks for the constant alertness of thoracic surgeons to their ever present danger.

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Developmental Anomalies of the Lungs

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To understand the malformations of organs it is necessary to know something about their normal development. The first indication of lungs appears in embryos of about seventeen to twenty somites at an ovulation age of twenty-four days (Streeter's Horizon XI). It consists of a median thickening of the ventral wall of the foregut just cranial to the liver diverticulum. In the beginning, therefore, the lungs develop at a very high level, near the junction of occipital and cervical segments. Within two days (Horizon XII, twenty-five to twenty-seven days, embryos of twenty-five to thirty somites), the primordium develops into a pear-shaped bulge of the ventral wall at the caudal end of a laryngotracheal groove. (Fig. 1, left upper sketch.) In another day or so (Horizon XIII, twenty-six to twenty-eight days, embryos of 4 to 5 mm.), this bulge gives rise to right and left lung buds with characteristic direction of growth, that of the right lung being more downward and that of the left more transverse (see series of sketches, Streeter, 1945). Meanwhile, as the lung buds elongate, the respiratory portion of the gut is being separated from the esophageal portion by lateral ingrowths of the surrounding mesoderm which meet progressively, in a cranial direction, to form a tracheo-esophageal septum. The arrows in Figure 1 indicate the level of separation of the two tubes. By the end of another two days (Horizon XIV, twenty-eight to thirty days, embryos of 6 to 7 mm.), the lung buds have elongated into the primary lung sacs or primary bronchi. (Fig. 1, left middle sketches.) Lateral views would show that they are growing dorsalward, crossing the plane of the esophagus, as well as downward.

On the thirtieth to thirty-second day (Horizon XV, embryos of 7 to 8 mm.) the five lobar bronchi appear as monopodial outgrowths of the primary bronchi. (Fig. 1, *U,M,L*, middle row of sketches.) From the thirty-second to the thirty-fourth day (Horizon XVI, 8 to 11 mm. embryos), the lobar bronchi merely elongate. Up to this time growth has been rather slow, nearly ten days having elapsed since the respiratory primordium first appeared. Then rather quickly the five lobar bronchi begin to branch, more or less dichotomously. By Horizon XVII (thirty-four to thirty-six days, embryos of 11 to 13.6 mm.) all segmental bronchi are present. In Horizon XVIII (thirty-six to thirty-eight days, embryos of 14 to 16 mm.) the subsegmental buds are beginning to appear (Fig. 2), and by the thirty-eighth to fortieth day (Horizon XIX, embryos of 17 to 20 mm.) all subsegmental bronchi are represented and many are undergoing further subdivision.

Details of these last three stages, covering the origin of the bronchopulmonary segments, may be found in a recent article by Wells and Boyden (1954). Suffice to say that these are the stages in which variations of the segmental bronchi first appear and study of embryos fails to support the "doctrine of the stem bronchus"—an axial structure with alternating dorsal and ventral branches. (See discussion of Aeby's theory in Chapters 1 and 9, Boyden, 1954.)

AGENESIS OF THE LUNGS

Obviously the factors that prevent the formation of the lungs must become effective not later than the period represented by Horizon XII (twenty-six days after ovulation), i.e., early in the second month of menstrual age.

Three different degrees of arrest of development may occur (Schneider, 1912): (1) complete absence of one or both lungs (agenesis);

(2) suppression of all but a rudimentary bronchus (aplasia); and (3) abortive growth (hypoplasia). Until the significant studies of Wilson and Warkany appeared (1949), it was difficult to explain these anomalies on other than a genetic basis. Recently, these authors have shown that agenesis can be produced experimentally in rat fetuses by depriving the mother of vitamin A. However, Warkany (1951) does not believe that in our American hospital patients there is sufficient malnutrition of this type to explain the agenesis that occurs. He suggests that diseases of the placenta or infectious agents such as rubella may so modify the vascular supply to the embryonic lung as to produce a nutritional deficiency that affects the chemistry of development.

Since this anomaly is being discussed by another writer in this series of articles (Dr. A. R. Valle) I shall merely note in passing that Oyamada, Gasul and Holinger (1953) have recorded seventy-three cases which clearly fall into the category of agenesis and aplasia, and then confine further remarks to the phase

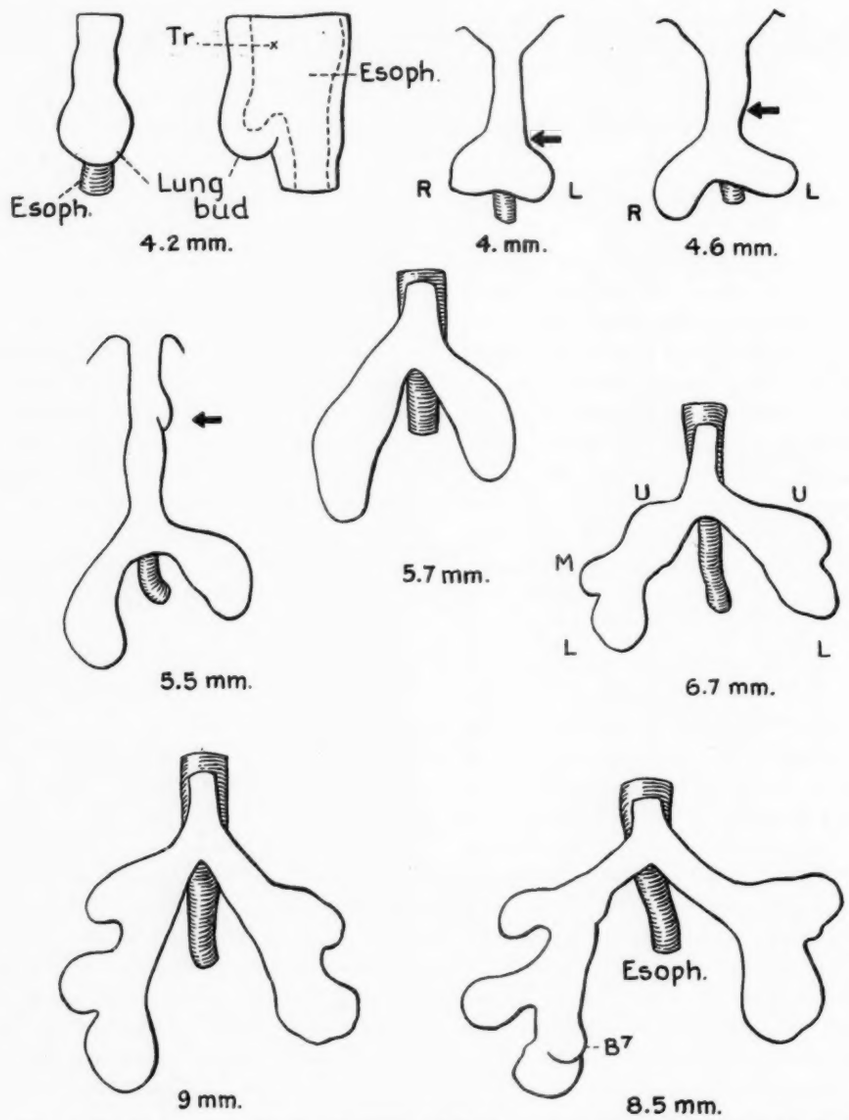

FIG. 1. Early stages in the development of the human tracheobronchial tree (after Heiss, 1919); covering Horizons XII to XVI of Streeter's age groups. The arrows indicate the level of separation of tracheal and esophageal tubes. *U,M,L*, upper, middle and lower lobar bronchi.

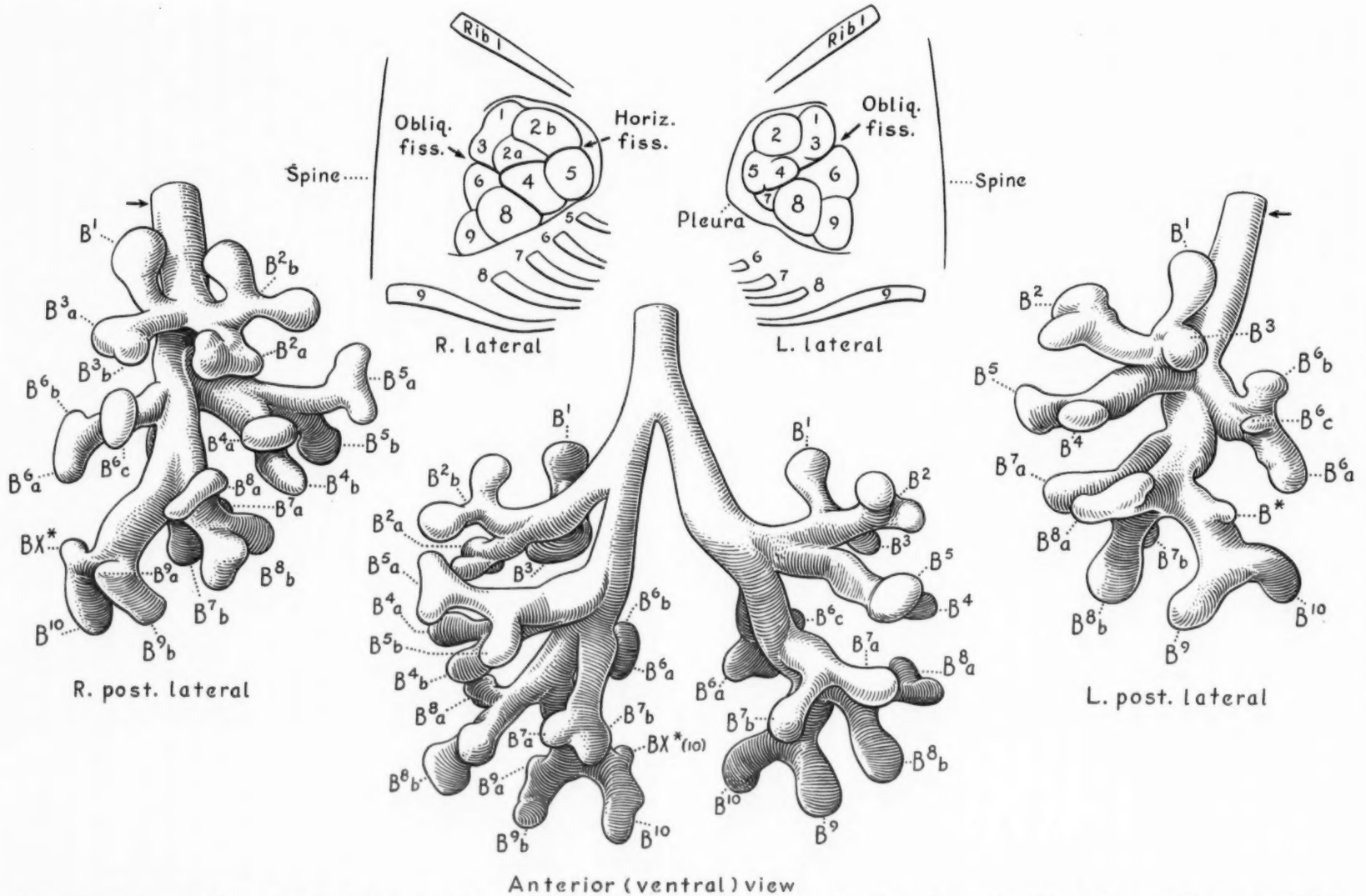

FIG. 2. Tracheobronchial tree of a 17 mm. human embryo of Horizon XVIII (after Boyden, 1954; dissection of pleural cavities and wax model by L. J. Wells). B^1, B^2, B^3 apical, anterior and posterior segmental bronchi; B^4, B^5 (right), lateral and medial segmental bronchi; B^4, B^5 (left), superior lingular and inferior lingular segmental bronchi; B^6, B^7, B^8, B^9, B^{10}, superior, medial, basal, anterior basal, lateral basal and posterior basal segmental bronchi. (Courtesy of the Blakiston Division of the McGraw-Hill Book Co.)

of the subject in which we have had special experience, namely, the structure of the persisting lung in cases of unilateral agenesis.

In the three cases of agenesis of the right lung that have come to our attention (Thomas and Boyden, 1951) the left lung exhibited many variants from the usual pattern. The first two cases had three lobes each, and the third none. The first had many variations of the segments, the second had a left eparterial bronchus, and the third had such vascular anomalies as coarctation of the aorta, persistent ductus arteriosus and a left postbronchial pulmonary artery. Therefore, even in surviving lungs there has been modification of normal development during the critical period of organ formation.

In addition to hypoplasia of a whole lung, there may be hypoplasia of just one lobe. A striking example of this is Hepburn's case (1925). Externally the right lung appeared to have only two lobes, but in the oblique fissure a flattened piece of tissue was found which adhered to the right upper lobe. This was supplied by a small bronchus, 10 mm. in diameter, which originated at the expected site of the middle lobe bronchus (in this case 26 mm. below the bifurcation of the trachea). Foster-Carter (1946) in discussing such hypoplastic lobes records a pertinent case of hyperplasia of the left lung in a male infant who had breathed only a few minutes. Here the anomaly was associated with absence of the left half of the diaphragm and herniation of the stomach and most of the intestines into the left pleural cavity. The right lung was expanded and normal, but the left bronchus led into a tiny lung about the size of a hazel nut. Bronchography revealed a branching bronchial system in the hyperplastic left lung.

In this case external pressures would seem to have provided the inhibitory factor. Similarly, in Hepburn's case a delayed origin of the bronchial bud could have given the upper and lower lobe bronchi such a head start that there was little room for arborization of a middle lobe bronchus. It will be recalled that irregular timing in the appearance of different buds is one of the characteristics of Horizon XVII.

ACCESSORY OR SUPERNUMERARY LUNGS

Of equal interest but of much rarer occurrence than agenesis are the rudiments of lung tissue that appear in ectopic positions. The most common site of origin is the trachea. A good example is Herxheimer's case (1901). He found a small functional "third lung" stemming from a tracheal bronchus 2.5 cm. down from the cricoid cartilage. This "sat above the lung on the right side" and had caused stenosis of the trachea when it pressed against its right side. Slightly different in position was the mass found by Stibbe (1929) in a forty-one year old female. This lay behind the manubrium in a crotch of the great vessels but was still attached to the right posterior wall of the trachea, an inch above the trifurcation. It was hollow and lined by ciliated columnar epithelium.

Such supernumerary lungs are not to be confused with bronchi of the apical lobe that have been displaced to the trachea (see section on displacement of lobar bronchi). Presumably the former arise from tracheal diverticula. Bremer (1932) found two sizable tracheal diverticula in young human embryos—a long one in a 16.5 mm. specimen and a somewhat shorter one in a 10.6 mm. embryo. Such diverticula may either branch or develop into tubular structures with walls that resemble the trachea. Chiari (1889) found five such specimens in 6,000 autopsies.

Probably the most impressive type of supernumerary lungs are the so-called Rokitansky lobes. Such isolated masses of lung tissue are located in the lower thorax. They occur most commonly on the left side above the diaphragm* and are usually separated from the tracheobronchial tree and pulmonary vascular system. Significantly these masses are subject to diseases that affect the main lungs.† About forty cases have been summarized by Davies and Gunz (1944). Their second specimen is an excellent example of this anomaly. It consisted of a pale, lymphoid-like mass (1½ by ¾ inches) which was associated with a left diaphragmatic defect and was attached by a pedicle to the upper face of the free margin of the defect. When sectioned it was found to consist of "fairly regular" lung tissue, but differed from an aerated lung in the greater thickness of the interlobular septa, in an excess of bronchioles over alveoli and in decreased vascularity.

A case of extraordinary interest is that of

* Bolck (1951) lists twenty-seven of forty-one cases in this position, and five more on this side, below the diaphragm.

† Findley and Maier (1951) have reviewed the blood supply of such accessory lungs as well as cases in which there is communication between greater and lesser circulations.

Scheidegger (1936). In a newborn male infant, a grayish red bilobed mass of lung tissue (52 by 45 by 38 mm.) occupied the lower left pleural cavity which in turn was filled with clear yellow fluid. As a result the heart was markedly shifted to the right. The right lung was three lobed but contained no air. The definitive left lung consisted of two diminitive lobes 25 and 27 mm. long, both atelectatic. The anomalous mass contained gas and was attached to the medial portion of the left dome of the diaphragm by a hollow stalk. Beneath the diaphragm, the stalk continued for 2 mm. to the stomach, joining it near the esophagus. Throughout, the stalk was lined with gastric mucosa which connected the cavity of the stomach with the bronchi at the base of the accessory lung. The author concluded that the anomalous mass was a "third lung that had grown out of the stomach."

This theory is not so improbable as one might think. At the time that the respiratory primordium first appears it lies adjacent to the esophagus and stomach. Perhaps this adjacent portion retained the potency to form lung tissue in the same way that lower derivatives of the foregut—from gallbladder to Meckel's diverticulum—retain the potency to form accessory pancreas. In this connection one might mention the case of Gans and Potts (1951) in which a mass of atelectatic lung parenchyma, compressing the left bronchus, was found attached (by hollow pedicle) to the left side of the esophagus at the level of the bifurcation of the trachea.

Another way of explaining these anomalies has been revived recently by Davies and Gunz (1944). They suggest that the lowest portion of the laryngotracheal groove (from which the lung buds develop) may become separated from the main primordium—owing to the rapid elongation of the foregut—and grow down with the esophagus and stomach to the level where the diaphragm will develop. Such a splitting or elongating of a primordium is not unknown, for the evidence is strong that double common bile ducts—the upper duct emptying into the stomach and the lower one into the duodenum —may develop by the separation and growing apart of portions of the hepatic diverticulum (Boyden, 1932).*

However, Cockayne and Gladstone (1917) consider that while these theories may account for the formation of accessory lungs in certain atypical situations, they do not offer an explanation for the preponderance of cases of lower accessory lung on the left side or account for the frequency with which such accessory lungs are associated with defective development of the diaphragm on the left side. They incline to another standing theory, namely, that lower accessory lungs are formed by adhesions taking place between the growing lung bud and the celomic epithelium, and that a portion of the adherent lung tissue becomes separated from the main part and takes on independent growth. They have found support for this hypothesis in a restudy of the early development of lungs and diaphragm, showing that in embryos from about 6 to 10 mm. length the lungs project below the pleuroperitoneal membrane into the peritoneal cavity, where they come into contact with such abdominal organs as the liver and stomach. The factor which they consider responsible for the adhesion taking place more commonly on the left side is the normal movement of the stomach to the left which also carries the lung buds to the left and narrows the left pleural cavity over that of the right, thus favoring adhesions. Until now a really detailed study of the successive stages in the development of the diaphragm has not been available. Such a study, however, is now in press (Wells, 1954) and one should be able to test this hypothesis in a way that has not been possible hitherto.

THE LEFT EPARTERIAL BRONCHUS

Since the time when Aeby first characterized the human lungs as being asymmetric—because of the presence of a right eparterial bronchus—and speculated that this condition had arisen through suppression of a corresponding left bronchus, students of the subject have searched in vain for a left eparterial bronchus

* In this connection mention should be made of the case of a five month old girl (Neuhauser and Elkins, *Am. J. Dis. Child.*, 83: 654–659, 1952) in which there was an anomalous tract, paralleling the esophagus, which connected the medial side of the right primary bronchus with the stem of the left hepatic duct. By means of this tract bile entered the lungs. The upper segment of the tract resembled trachea, the large middle segment the esophagus, the lower segment the bile duct. Two explanations are offered: (1) the very early fusion of the lung bud and hepatic diverticulum, followed by subsequent drawing out of the anomalous union; (2) the early duplication and subsequent elongation of that part of the foregut between the laryngotracheal groove and the hepatic diverticulum.

in man. Through good fortune, we have encountered five cases in the Minnesota laboratory in the last eight years. Four of these were in cadavers and one in the sixteen-day old twin baby girl mentioned previously as having agenesis of the right lung. Incidentally, there was no agenesis of the lung of the identical twin, suggesting that in these two siblings the defects were of environmental but not genetic origin.

In such specimens the feature which strikes the observer first is the ectopic position of the large left pulmonary artery. This enters the left lung between two bronchial stems that arise separately from the left primary bronchus. The upper (or eparterial) stem supplies the left apical anterior segment (B^{1+3}), and may enter a portion of the anterior segment (B^2). Therefore the left eparterial is not exactly comparable to the right eparterial bronchus. The lower stem supplies the anterior (B^2) and lingular segments (B^4 and B^5). In two cases a supernumerary fissure led to the pulmonary artery from the anterior margin of the lobe (Boyden, 1949).

What is the etiology of this anomalous bronchus? From our study of embryonic lungs, we infer that about Horizon xv (cf. right middle sketch of Fig. 1) two left upper lobe buds (instead of one) must have arisen from the left primary lung sac. Since only one case was found in 100 consecutive dissections, it is assumed that this anomaly has an incidence of not more than 1 per cent. It is important surgically, however, that it be recognized when present.

DISPLACEMENT OF LOBAR BRONCHI

In addition to the foregoing cases it occasionally happens that a single lobar bronchus develops at a lower or higher point than usual on the primary lung sacs. Huizinga and Smelt (1949) present a bronchogram of such a case (their Fig. 108) in which the whole right upper lobe bronchus originates just above the normally placed middle lobe bronchus. In a second case (their Fig. 17*e*) both right upper and middle lobe bronchi arose from a common stem at the usual site of the middle lobe. Sweet records a surgical case in which the reverse condition occurs. There the middle lobe bronchus arose from a normally placed right upper lobe bronchus, either from its main trunk or from the proximal part of the anterior segmental bronchus (Boyden, 1954, Chapter 5). Finally, the whole right upper lobe bronchus may originate from the right lateral wall of the trachea, as in certain Ungulates.

DISPLACEMENT OF SEGMENTAL AND SUBSEGMENTAL BRONCHI

The lesser variations in the patterns of the bronchial trees are due primarily to displacement of segmental and subsegmental bronchi. Although lesser in degree than those of other categories, they are nevertheless of great practical importance in the resection of bronchopulmonary segments. The displacement occurs at the time that the segmental and subsegmental buds appear, namely, in embryos of Horizons xvii to xix (thirty-four to forty days after ovulation). It takes the form of buds originating at atypical sites on the tree. Only a few of the more significant variations will be mentioned here. (For the remainder see Boyden, 1954.)

One of the most confusing variants is the one which supplies all or part of the apical segment and arises on the right side of the trachea or from the lateral wall of the right primary bronchus before the lobar bronchus is given off. It is the displaced variety of what we have termed the "pre-eparterial bronchus." It is not a supernumerary bronchus but merely a displaced apical ramus or apical bronchus (cf. Plate 1, Boyden, 1952).

Similarly, one of the upper lobe bronchi may originate at a lower level. For example, the right anterior bronchus (B^2) may arise from the middle lobe stem. Such a variation we have termed "the posteparterial bronchus" (cf. Fig. 2 Boyden and Hamre, 1951). It, too, is not supernumerary but merely a displaced portion of the upper lobe bronchus since it distributes to the territory of B^2 in that lobe.

Another example of displacement may be seen in Figure 2 of this article. Normally the left medial basal bronchus (B^7) and left anterior basal (B^8) arise from a common stem. But in 7 per cent of 100 specimens B^7 arises alone, at a higher level on the tree (see bronchi labeled *7a* and *7b* in the right hand portion of the central sketch of Fig. 2). The same sketch (left hand side) illustrates one of four types of right medial basal bronchus. In this type II the two subsegmental buds are so oriented that they will supply only the anterior surface of the right lower lobe (cf. Plate 4 of Ferry and Boyden, 1951).

Again, the posterolateral view of the left

lower lobe in Figure 2 (sketch on the extreme right) reveals the absence of B^2a, the posterior ramus of the anterior segment. When present (65 per cent) it is a site in which lung absence of the left upper lobe most frequently occurs. The surface view of the same lung confirms the absence of this ramus in the embryo, for B^2 fails to reach the oblique fissure (see left upper central sketch).

From these few examples it is apparent that such variations develop during the period when the segmental and subsegmental buds are being formed. What is not clear is the cause of these variations. Probably they are due to minor environmental factors of intrauterine life, for Ando (1951) has shown that even in monozygotic twins the respective right or left lungs have slightly different patterns.

SUPERNUMERARY FISSURES AND CONGENITALLY FUSED LOBES

One of the most common anomalies of the lungs is the supernumerary fissure. A good account of these is presented by Mueller (1928) and Foster-Carter's discussion of abnormalities of lobation (1946). Contrary to common belief such fissures do not always separate segments but may enter subsegmental or even smaller interbronchial planes.

Perhaps the most common site for a supernumerary fissure is the line between the medial basal and anterior basal segments (B^7 and B^8) of the right lower lobe. It partially segregates a cardiac or infracardiac lobe. This corresponds to the free cardiac lobe of quadrupedal mammals but should not be considered atavistic since it in no wise differs from anomalous fissure formation in other portions of the lungs. Dévé (1900) found traces of it in 35 per cent of 180 human lungs. A similar incisure of varying depth was observed by Smith and Boyden (1949) in 38 per cent of fifty injected right lungs. All of them would have been noted in surgical exploration, and some in roentgenologic examination. A comparable fissure occurs in the left lung, but infrequently (cf. Plate XI, Boyden, 1954).

Another common fissure is the one that separates the so-called "dorsal lobe of Nelson" (1934). This fissure segregates, to a greater or lesser degree, the superior segment of the right or left lower lobe. Long before Nelson, this fissure was found by Dévé in forty right lower lobes and fourteen left lower lobes. (In twelve cases the fissure was bilateral.) He called the segregated portion the "posterior lobe." Curiously enough such horizontal fissures cannot be depended upon to follow intersegmental planes. In a case reported by Ferry and Boyden (their Plate 6) the fissure developed not between superior and subsuperior segments but between subsuperior and lateral basal zones.

A third common form is the left horizontal fissure. This subdivides the left upper lobe into two more or less equal portions, the lower of which is called the "left middle lobe." But it is not always comparable to a right middle lobe. Four types (Boyden, 1949) have been described: (1) a true middle, separating normal upper and lower division segments; (2) a compressed lingular; (3) an expanded lingular; and (4) the ectopic pulmonary type. This last always separates the sector of an eparterial bronchus from the remainder of the left upper lobe. It also illustrates Foster-Carter's category of fissures that are due to displaced blood vessels: such as Monod's case (1911) of a subclavian artery that split the apex of the right lung to a depth of 3 cm., and second, the fissures that separate the lobe of the azygos vein.

Both normal and supernumerary fissures develop during the period when the segmental and subsegmental buds first appear. In the surface views of the 17 mm. human embryo in Figure 2 both oblique and horizontal fissures are evident as deeper crevices lying between the lobular elevations formed by the segmental buds of the bronchial tree. In a somewhat older embryo of 20 mm., presented by Wells and Boyden (their Fig. 3g) there is a supernumerary fissure separating the "left middle" lobe from superior division bronchi. This early appearance of fissures suggests that the cutting in of visceral pleura around bronchial buds may depend partly upon the prominence of given buds at the time of their formation. That is, a precociously appearing bronchus might favor the development of an accessory fissure. Subsequent growth, however, may modify the situation; for it is well recognized that peripheral portions of the right horizontal fissure, for example, are frequently found to be congenitally fused, while the deeper, hidden portions remain open and lined with a pleural investment.

This brings us to the subject of congenital fusion of lobes. This again is one of the most common anomalies. Kent and Blades (1942)

found the horizontal fissure absent in 21 per cent of 277 lungs and incomplete in 67 per cent more. The oblique fissures were incomplete in 30 per cent of both right and left lungs.

LOBE OF THE AZYGOS VEIN

This striking malformation of the apex of the lungs has been known since 1777 when it was first described by Wrisberg in the cadaver of a three year old boy. It is noteworthy that the first case was a bilateral one, for as late as 1952 its occurrence on the left side has been denied (Kane). In 1953, Weston reported a case of his own and ten others from the literature. However, the anomaly is much more common in the right lung. Bluntschli (1905) quotes Professor Boström as having found seventeen azygos lobes in 1,600 dissections. On the other hand, we have been favored with only one in almost 500 dissections. Schmitz-Cliever estimates that it occurs in 0.3 per cent of all x-rayed lungs.

The lobe in question is a medial, split-off portion of the apex caused by the descent of the right (or left) posterior cardinal vein within its drawn-out fold of costal pleura (the mesoazygos). Evidence that it is a phenomenon of the mechanics of growth is found in the fact that the apical bronchi are bent almost double along the line of contact with the vein. The right posterior cardinal vein, at its proximal end, becomes the arch of the azygos vein. Hence the name of the lobe.

As the heart "descends" in development, it drags the vein down into the apex. This process may be supplemented by the upward growth of the apex; for a glance at Figure 2 indicates that as late as the thirty-seventh day the apical portion of the lung has not grown higher than the second rib. Until lately, there has been no satisfactory explanation of why a vein which lies medial to the adult lung should have cut into it laterally. Recently (cf. Boyden, 1952) Professor L. J. Wells has advanced the theory that since the posterior cardinal veins originally lie lateral to the pleuropericardial canals—which latter extend upward from the pleural dome—any delay in closure of these canals would leave the vein in a position to descend upon the apex.

The angle at which the vein descends determines the size of the wedge and the particular bronchi that will be segregated. The line of descent may pass quite obliquely from the lateral side of the apex toward the hilum, it may lie approximately in a vertical plane (thereby splitting the apex) or it may descend medial to the apex. Roentgenologically, the mesoazygos appears as a curved descending line having its concavity toward the vertebral column and expanding at its lower end to enclose the "drop-like" azygos vein.

With the advent of segmental anatomy, it has been possible to identify the bronchial supply of the lobe. Either the apical or the anterior ramus of the apical segment (B^1a or B^1b) is always present. In the larger lobes both may be present or B^1a and B^3a, the apical rami of the apical and posterior segments (Boyden, 1952). In the article quoted, a detailed account of the attachments of the mesoazygos is presented.

The clinical importance of the mesoazygos is at least twofold. First, it must not be confused with pathologic markings in the apex. Second, its presence or absence should be verified before operating on the upper lobe lest, in cases of adherent mesoazygos, the vein be ruptured unwittingly with ensuing hemorrhage.

"SEQUESTRATION" OF BRONCHI

The etiology of "cystic disease" of the lungs is one upon which few investigators agree. Embryologically there is little evidence, if any, supporting an early separation or constriction of portions of the developing bronchial tree. That such may occur in late fetal stages or at birth through pathologic processes, or otherwise, seems more probable. Curiously enough, cystic disease is often associated with the presence of a large accessory pulmonary artery arising from the lower thoracic aorta or even from lower intercostal or subdiaphragmatic arteries (inferior phrenic and celiac). Because of this, Pryce (1946, 1947), Bruwer and associates (1950) and Kergin (1952) have related the two anomalies causally, postulating that in early embryonic stages the terminal buds of the growing bronchial tree have been "captured" by systemic arteries that "anchor the mass while the lung is undergoing developmental shifts." It is then suggested that the resulting traction results in formation of cysts and sequestration of the captured mass.

This seems to be a plausible explanation until embryonic processes are analyzed. First, accessory arteries to the base of the lungs occur in the absence of cysts, and vice versa (cf. Fig. 120, Boyden, 1954). Second, the distribu-

tion of an accessory artery is often such that mechanically the artery could not have produced a traction defect (cf. Fig. 123, Boyden, 1954). Third, arteries do not exert traction upon viscera in developmental stages. Instead, there is either a gradual shifting of an artery along the wall of a major vessel like the aorta (either through differential growth or selection of plexiform channels), or new arteries develop successively, to keep pace with a "descending" organ.

Such a process occurs, for example, in the development of the bronchial arteries. In early stages the developing lung buds, trachea and esophagus are surrounded by a common "splanchnic plexus" supplied by a series of small segmental arteries from the ventral side of the paired dorsal aortas. These arteries of the upper cervical region are the precursors of the bronchial arteries. Tobin (1952) has shown that as the lung grows downward the more cranially situated segmental arteries drop out and others, formed lower down, take their place. In a subsequent stage the bronchial arteries are found to arise from the left aorta, from the subclavian artery, the highest intercostal and even from the right internal mammary—thus explaining some of the atypical origins of the bronchial arteries recorded in adults. The lowest of this series of aortic branches are the accessory pulmonary arteries frequently associated with cysts. One may assume that once having established connection with the lower portion of the growing lung they keep pace with the downward growth of the lung by shifting downward themselves, until finally they may arise from the aorta just before it pierces the diaphragm.

Another example of this process is the blood supply to the stomach. Originally it arises from the cervical region of the embryo, but gradually it shifts its position along the ventral wall of the aorta until it becomes the definitive celiac artery—all this without having "captured" the stomach.

GROSS ANOMALIES OF THE PULMONARY VESSELS

Arteries. In addition to the accessory pulmonary arteries discussed in the preceding section, i.e., those originating from the thoracic aorta below the hilum of each lung, pulmonary arteries may arise atypically from the derivatives of the embryonic aortic arches. Findlay and Maier (1951) have listed twenty-five such cases (their Fig. 1), as follows: ten from the ascending aorta and arch of the aorta, four from the innominate artery, two from the right subclavian, five from the left subclavian, and four from the descending aorta above the hilum of each lung. Such aberrancies are usually associated with malformations of the heart and developmental anomalies of the aortic arches.

Another recent summary may be found in the article by Castellanos and Garcia (1951). A classic case is that of Ingalls (1932) in which the stem of the right pulmonary artery arose from the right ductus arteriosus near the point where the latter joined the persisting right fourth aortic arch.

Veins. In the preceding section, reference was made to the existence of a primitive splanchnic plexus which surrounds the developing lung buds, trachea and esophagus. At an early embryonic period this plexus drains into the anterior cardinal veins. Thus it is possible, under abnormal conditions, for the pulmonary veins to retain connection with the derivatives of the anterior cardinal. Brantigan (1947), in summarizing Brody's and other reports of 106 such cases, found that the drainage from the lungs passed wholly into the right atrium or its tributaries in 36 per cent and partially in the remaining 64 per cent. In the latter cases the most common site, in order of frequency, was the superior vena cava, the right atrium and the left innominate vein. Right pulmonary venous anomalies occurred twice as often as left ones. Other sites of drainage were the coronary sinus, inferior vena cava, azygos vein, left subclavian vein, portal vein and left persistent superior vena cava. Young (1947) has discussed the drainage into the portal vein.

Anomalous drainage into the right atrium, vena cavas and coronary sinus is differently explained than drainage into derivatives of the anterior cardinal veins. Auër (1948) has shown that in a series of 2 to 7 mm. human embryos, there are both caudal and cranial evaginations of the sinu-atrial region into the dorsal mesocardium. The cranial type is the one that usually gives rise to the stem of the pulmonary vein that makes contact with the capillaries of the splanchnic plexus. The caudal type normally disappears, but persistence of it may lead to the formation of anomalous pulmonary veins that empty either into the coronary sinus, the superior or inferior vena cava or the right atrium.

Mention should also be made of the variations in the mode of entrance of the pulmonary veins into the left atrium. This is important from the standpoint of new operative procedures in which the pulmonary veins are ligated intrapericardially. Healey and Gibbon (1950) report that in 3 per cent of 184 specimens, the right lung drained into a common right pulmonary vein before emptying into the left atrium. On the left side the figure rose to 25 per cent. Conversely, the right pulmonary may be represented by three veins emptying side by side. In three cases by Healey and Gibbon, and two by Brantigan, the three veins came respectively from the three lobes of the right lung, but in the case of Ferry and Boyden, the middle vein drained not only a portion of the middle lobe, but also much of the lower lobe. Therefore, in intrapericardial ligation of such cases, it is not safe to assume that the three veins drain the respective lobes.

Arteries and Veins of the Bronchopulmonary Segments. Variations in the blood supply and drainage of the segments of the lungs are so numerous that they cannot be easily summarized. Accordingly interested readers are referred to the chapters dealing with variations in the individual lobes of the lungs (Boyden, 1954).

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Agenesis of the Lung

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AGENESIS, congenital absence, of a lung or lungs is a condition which has long been recognized. The first case on record was cited by Morgagni in 1762. The diagnosis was made at autopsy in the early cases reported. However, as diagnostic aids such as x-ray, bronchography, bronchoscopy and exploratory thoracotomy have come into use, the condition is being discovered more often in living persons. From a review of the recent literature, agenesis of the lung appears to occur with sufficient frequency to merit consideration in the differential diagnosis of certain chest conditions.

According to Schneider[2] there are three main types of this abnormality: (1) true aplasia in which there is no trace of the lung, bronchus or vascular supply on the affected side; (2) conditions in which the bronchus is represented by a small outpocketing from the trachea and is supported by a ring of cartilage; (3) extreme hypoplasia, rather than aplasia, in which the bronchus is fully formed but is reduced in size and ends in a fleshy structure without lobes which lies within the mediastinum. The microscopic picture lies somewhere between rudimentary lung tissue and extreme hypoplasia.

A chart follows which lists 120 cases of agenesis of the lung, 119 collected from the literature and one additional original case. Such pertinent data as were available are presented with each case. It should be mentioned that this chart includes only those cases of complete agenesis of both lungs, and those in which the amount of lung tissue present on the affected side did not exceed that of Schneider's type III.

DIAGNOSIS

Usually the patient with agenesis of the lung has no acutely distressing symptoms; however, difficulty in breathing, wheezing, cough, expectoration and cyanosis are common. Patients with this condition are prone to ordinary respiratory infections, but many patients seem to have no symptoms and live normal lives.

Physical examination usually reveals asymmetry of the chest, flattening of the involved side, and lagging of respiratory movements in the same area. The trachea is often found shifted toward the side of the missing lung. The mediastinum and heart are displaced to the abnormal side, producing dullness on percussion and absence of breath sounds, particularly at the base. In some cases the heart is so rotated that its sounds can be heard on the posterior chest wall. A simulated dextrocardia is found in cases with agenesis of the right lung. Normal physical findings, especially in the upper part of the defective side are often encountered, due to the marked herniation of the existing lung.

X-ray studies usually show the affected side to be dark and opaque. The intercostal spaces are narrowed and the diaphragm is elevated. A characteristic feature is the protruding across the midline of the hypertrophied remaining lung. The vertebral column looks more clearly defined than usual. The heart can be seen on the side of the missing lung, near to the chest wall. Laminograms are an important aid in bringing out all these features. Bronchograms give valuable information about the position of the trachea, the bronchial tree and the degree of herniation. In some cases they will show the bronchial block where the main bronchus of the missing lung should be branching off from the trachea. Also, at times, it is possible to differentiate between Schneider's types I, II or III on the basis of the bronchogram.

Angiocardiograms will outline the heart, great vessels of the mediastinum and congenital malformations, if present. Also, they show the relationship between the respiratory and cardiovascular system. For example, in Maier and Gould's case, angiography revealed the vascular compression of the airways which was confirmed at thoracotomy. The anomalous course of the left pulmonary artery and the aorta exerted sufficient pressure on the lower trachea to cause the patient to die of asphyxiation. This vascular compression of the airways may not be obvious from postmortem examination alone

Agenesis of the Lung

References	Sex and Age	Side	Findings
1. Cited by Morgagni: *De sed. et caus. morb. epist.*, 4: 136, 1762	M, young	Right	Diagnosis made at autopsy
2. Haberlein: *Abbandl. der rom. kk. Josephin. med. u. chir. Akad. zu Wien.*, 1: 271, 1787	M, 20 yr.	Left	No left pulmonary vessels or bronchus; left thorax filled with watery fluid; right lung normal
3. Pozze cited by Meckel, J. F.: Handbuch der Path. u. Anat., vol. 1. Leipzig, 1812		Left	Diagnosis made at autopsy
4. Sommering: *Zusatze. zu Bailles Anat. d. Krankh. Baues etc.*, p. 445. Berlin, 1820	Child	Right	Diagnosis made at autopsy
5. Bell: Anatomy and Physiology of Human Body, 5th ed., 1827	Female fetus	Right	Trachea divided into three branches at hilum of left lung; left lung not lobed; pulmonary artery divided into a right branch and ductus arteriosus; one vein emptied into left auricle; autopsy findings
6. Bell: Ibid.	M, young	Left	Left hydrothorax
7. Hein: *Wchnschr. f. d. ges. Heilk. Berl.*, p. 536, 1827	M, 6 wk.	Right	Right pulmonary vessels absent; rudimentary right bronchus; defect in ventricular septum; patent foramen ovale; pulmonary artery closed at base of heart; left lung supplied by ductus arteriosus
8. Mashka: *Allg. Wien. med. Zeitschrift*, p. 78, 1862.	Premature child lived 2 hr.	Right	Heart in right side of thorax; bronchus represented by pea-sized sac; right pulmonary vessels absent; left lung not lobed; esophagus ended blind at mid-point
9. Gruber, Oester: *Ztschr. f. prakt. Heilk.*, 16: 7, 1870	F, stillborn	Right	No right pulmonary vessels or bronchus; left lung unilobar; with only one pulmonary vein
10. Ponfick: *Virchows Arch. f. path. Anat.*, 50: 633, 1870	F, 5 days	Right	Asymmetric thorax; small bud of lung tissue at end of short bronchus (Schneider's type III) patent ductus arteriosus; intraventricular septal defect; weak heart musculature
11. Herrero, F.: *Corresp. méd., Madrid*, 9: 372, 1876	M, 65 yr.	Left	Undivided trachea continuous with right bronchus; right lung enlarged
12. Stein, J. (1878) cited by Madigan: *Tubercle*, 22: 144, 1941	Infant, 6 wk.	Right	Pulmonary vessels completely absent; rudimentary right bronchus
13. Haberlein cited by Madigan: *Tubercle*, 22: 144, 1941	M, 24 yr.	Right	No right bronchus; pulmonary artery entered undivided into left lung; right hydrothorax; left lung enlarged with two bronchi entering it
14. Theremin: *Rev. mens. d. mal. de l'enf.*, 25: 554, 1884	11 days	Left	Trachea continuous with right bronchus; small cartilaginous nodule at site of left bronchus; right lung unilobar; no pulmonary veins entered left auricle; united to form a large vessel communicating with a distended vena azygos
15. Ibid.	F, 127 days	Left	Trachea continuous with right bronchus; left pulmonary vessels absent; right lung imperfectly separated into two lobes; vein from right lung emptied into vena azygos

References	Sex and Age	Side	Findings
16. Gruber, W.: *Virchows Arch. f. path. Anat.*, 102: 11, 1885	F, fetus	Left	Trachea divided into three branches in hilum of right lung; right lung not lobed; pulmonary artery divided into a right branch and ductus arteriosus; one vein emptied into left auricle
17. Munchmeyer: *Deutsche med. Wchnschr.*, p. 295, 1885	M, 2 yr.		Diagnosis made at autopsy
18. Wollmann (1891) cited by Bohnholtzer: *Beitr. z. path. Anat.*, 101: 614, 1938	24 yr.	Left	Short left bronchus present; diagnosis made at autopsy
19. Schmidt, H.: *Virchows Arch. f. path. Anat.*, 134: 25, 1893	M, stillborn	Both lungs absent	Ten tracheal rings only; trachea fused with esophagus; pulmonary artery into aorta; no pulmonary veins; patent foramen ovale
20. Miller: *Trudi, Obsh. dietsk. vrach., Mosk.*, 3: 32, 1894–95	M, 4 wk.	Left	Pea-sized left lung attached to a narrow bronchus; pneumonia of right lung
21. Ibid.	M, 6 wk.	Left	Left lung cherry-sized, attached to narrow bronchus
22. Ibid.	F, 2 days	Left	Left lung 2 cm. in diameter; attached to narrow bronchus
23. Tichomiroff: *Internat. Monatschr. f. Anat. u. Physiol., Leipz.*, 12: 24, 1895	F, 24 y.	Left	No left bronchus; trachea divided into three bronchi before entering the right lung
24. Gross, W.: *Zieglers Beitr. zur Path.*, 37: 487, 1895	M, 5 mo.	Left	Blind left bronchus; left pulmonary vessel absent; right lung enlarged no lobulation; other lesions included left-sided hypoplasia of face, dermoid of left eye, etc.
25. Hanson, R.: *J. A. M. A.*, 37: 701, 1901	F, full-term lived 15 min.	Left	Bronchus very short; heart on right side; right lung smaller than normal; diaphragm lacking on left side with some abdominal viscera in pleural cavity
26. Oberwarth: *Jahrb. f. Kinderh.*, vol. 60, 1904	F, 1 yr.	Right	Diagnosed at autopsy
27. Findlayson: *Proc. Anat. Soc. Gr. Brit. & Ireland, Lond.*, vol. 38, 1907	Infant, lived few hours after birth	Right	Trachea ended in left bronchus; pulmonary vessels undeveloped; left lung hypertrophied
28. Ellis, A. G.: *Am. J. M. Sc.*, vol. 154, 1917	M, 8 yr.	Left	Absent pulmonary vessels; right lung enlarged with five lobes; hydropericardium and vegetations on mitral valve
29. Tebbutt, A. J.: *M. J. Australia*, 2: 430, 1918	M, 12 yr.	Left	Heart in left thorax; pulmonary artery divided into two branches before entering right lung; pericardial adhesions; endocarditis of mitral and aortic valves
30. Jarisch: *Wien. klin. Wchnschr.*, 3: 736, 1919	M, 29 yr.	Left	No pleura; left bronchus present as a short stump; mediastinum displaced to left with heart against left chest wall; slight pericardial fluid; enlarged imperfectly fissured right lung showing bronchopneumonia

References	Sex and Age	Side	Findings
31. Levy, C. S.: *Am. J. M. Sc.*, 159: 237, 1920	M, 49 yr.	Left	No left bronchus or pulmonary vessels; right lung enlarged; lobular pneumonia; also had syphilis
32. Muhamed, K. S.: *Indian M. Gaz.*, 58: 262, 1923	F, 19 yr.	Left	Thickened upper left pleura; trachea entered right undivided; heart displaced to left; pericardium full of blood; two thymus glands; one in left pleural cavity; ruptured spleen and liver
33. Allen and Affelback: *Surg., Gynec. & Obst.*, 41: 375, 1925	F, stillborn	Bilateral	Trachea ended blindly; pulmonary artery entered aorta; patent foramen ovale
34. Dannheiser, F.: *Beitr. z. patb. Anat.*, 76: 87, 1926	M, 34 yr.	Left	Enlarged right lung entered into left pleural cavity; trachea had 26 rings and divided into two branches both entering right lung; heart displaced to left; died of skull fracture
35. Heerup, L.: *Hospital*, 70: 1165, 1927	F, 72 yr.	Left	Left thorax filled by large heart, pericardium, great vessels and hypertrophied right lung; died of cerebral hemorrhage and bronchopneumonia
36. VonEicken: *Med. Klin.*, 23: 1836, 1927	F, adult	Left	Small blind pouch on left side of trachea
37. Bonninger, M.: *Med. Klin.*, 24: 1258, 1928	M, 37 yr.	Right	Right bronchus ended blind 12 cm. from carina in two small pea-sized sacs
38. Gilkey, H. M.: *J. Missouri M. A.*, 25: 296, 1928	M, 6 mo.	Right	Right lung absent; mediastinum and trachea displaced to right
39. Welsch, K.: *Frankf. Ztscbr. f. Patb.*, 36: 192, 1928	M, 58 yr.	Right	Right lung, right pulmonary vessels, and right vagus nerve absent; chest asymmetrical; heart and mediastinum shifted to right; died following automobile accident
40. Lochow: *Zentralbl. f. allg. Patb. u. patb. Anat.*, 46: 170, 1929	Infant, 5 mo.	Left	No left bronchus; one pulmonary artery
41. Bonninger, M.: *Med. Klin.*, 27: 1568, 1931	M, 27 yr.	Right	Right bronchus ended blindly 4 cm. from carina
42. Finner, L.: *Clifton M. Bull.*, 18: 35, 1932	M, 22 mo.	Right	Complete absence of right lung; peanut in trachea; mediastinum displaced to right; emphysematous left lung; autopsy findings
43. Minne and Gernez. *Ann. d'anat. patb.*, 10: 503, 1933	F, stillborn	Left	Heart filled left chest; slight amount pericardial fluid; right lung enlarged without fissures; exencephaly
44. Wehn and Clemens (1934) cited by Bohnholtzer: *Beitr. patb. Anat.*, 101: 614, 1938	F, newborn	Left	No left bronchus; no left pulmonary vessels; atresia of larynx; tracheoesophageal fistula
45. Hepner: *Arcb. f. Kinderb.*, 103: 92, 1934	F, 3 mo.	Left	No left pulmonary vessels; high left diaphragm; right lung enlarged, incompletely fissured; heart filled left thorax; accessory spleen
46. Knott: *Ztscbr. f. Kinderb.*, 56: 338, 1934	M, 5 wk.	Right	Right bronchus absent, dextrocardia and mediastinum displaced to right; hypertrophied left lung; bronchopneumonia

References	Sex and Age	Side	Findings
47. Dyson, J. E.: *Iowa M. Soc. J.*, 24: 442, 1934	F, 6 mo.	Left	No left pulmonary vessels or bronchus; right lung showed edema, emphysema and interstitial pneumonia
48. Toni, D.: *Clin. pediat.*, 16: 241, 1934	F, 4 mo.	Right	Heart and mediastinum displaced to right; hypertrophied left lung; bronchopneumonia
49. Mitchell, H. E.: *Obio State M. J.*, 32: 950, 1936	F, 2 yr.	Right	Right lung and right pulmonary vessels absent; mediastinum shifted to right; right main bronchus ended in blind pouch; patient died after aspirating peanuts and gum into trachea
50. Elward: *Radiology*, vol. 27, 1936	M, 43 yr.	Left	Marked hypertrophy of right lung; rudimentary left lung; bronchi incarcerated in mass of adhesions; very small left pulmonary artery
51. Hurwitz and Stephens: *Am. J. M. Sc.*, 143: 81, 1937	F, 7 wk.	Left	Absent left lung; small bud of tissue at end of bronchus; vein from it entered right vena azygos; microscopic section showed fetal lung tissue; right lung hypertrophied
52. Reinhoff, W. E.: *J. Thoracic Surg.*, 6: 254, 1937	M, 50 yr.	Left	Small pouch at place of left bronchus; no left pulmonary vessels; left innominate vein entered into right auricle
53. Ibid.	M, 4 mo.	Right	No right bronchus; no right pulmonary artery; patent foramen ovale; patent intraventricular septum
54. Bohnholtzer, E.: *Beitr. path. Anat.*, 101: 614, 1938	Infant, premature	Right	No tracheal rings; no right bronchus; no right pulmonary vessels; patent ductus arteriosus; patent foramen ovale
55. Wasmuth, K.: *Frankf. z. Path.*, 52: 517, 1938	M, 4 wk.	Right	22 tracheal rings; no right bronchus; no right pulmonary vessels; patent ductus arteriosus; patent foramen ovale
56. Ibid.	Infant, 3 mo.	Right	Small rudimentary right bronchus; no right pulmonary vessels; patent ductus arteriosus
57. Jamuni and Ellis: *Am. J. M. Sc.*, 196: 824, 1938	M, premature	Left	Rudimentary left bronchus ending blindly
58. Fomijne, P.: *Nederl. tijdschr. verlosk. en gynaec.*, 82: 5482, 1938	F, 19 yr.	Left	Diagnosed during life; left chest smaller than right; heart and mediastinum shifted to left; bronchogram showed only rudimentary left bronchus; left arm smaller than right; left thumb rudimentary
59. Yampolsky and Fowler: *Arch. Pediat.*, 55: 293, 1938	M, 2 yr.	Right	Right bronchus 1 cm. in length; rudimentary right lung; hypertrophic left lung; heart greatly enlarged; died of bronchopneumonia
60. Killingworth and Hibbs: *Am. J. Dis. Child.*, 58: 571, 1939	F, 10 days	Right	No right bronchus; large right auricle; patent ductus arteriosus pulmonary stenosis; patent foramen ovale
61. Heemstra: *Nederl. tijdschr. verlosk. en gynaec.*, 83: 2750, 1939	F, 4 wk.	Right	Absent right bronchus; diagnosis made during life and confirmed at autopsy

References	Sex and Age	Side	Findings
62. Choisser and Bloedorn: *New Internat. Clin.*, 2: 223, 1939	M, 43 yr.	Left	Left bronchus very narrow; left pulmonary artery 0.5 cm. in diameter; enlarged right pulmonary vessels; malformed left auricle; mitral stenosis
63. Stokes and Brown: *M. J. Australia*, 1: 29, 1940	F, 12 yr.	Left	Diagnosed during life; rapid breathing; dull percussion sound and no breath sounds right side; heart in right chest
64. VanLoon and Diamond: *Am. J. Dis. Child.*, 62: 584, 1941	F, 3½ yr.	Right	Diagnosis made during life; chest asymmetric; heart and mediastinum shifted to right; right diaphragm elevated
65. Madigan, D. G.: *Tubercle*, 22: 144, 1941	F, 23 yr.	Left	Diagnosis made during life; chest asymmetric; slight dyspnea on exertion; absence of breath sounds on left side of chest; bronchoscopy revealed abnormally small left bronchial tree; x-ray showed left side reduced and opaque
66. Castellanos and Pereiras: *Bol. Soc. cubana de pediat.*, 14: 268, 1942	F, 10 yr.	Left	Left chest smaller than right; breath sounds absent over left chest; slight dyspnea on exertion; diagnosis made during life
67. Ibid.	F, 10 yr.	Right	Chest asymmetric; ribs on right side closer together than those on left; heart and mediastinum shifted to the right; diagnosis made during life
68. Ibid.	Infant, 1 day	Left	
69. Gartside, V. O. B.: *Brit. J. Radiol.*, 16: 69, 1943	M, 7 yr.	Left	Diagnosis made during life; chest asymmetric; heart and mediastinum shifted to left; breath sounds absent over left chest
70. Olcott and Dolley: *Am. J. Dis. Child.*, 6: 776, 1943	F, 2 mo.	Right	Enlarged left lung; trachea formed almost direct line with left bronchus; autopsy finding
71. Selander cited by Wexels: *Thorax*, 6: 171, 1951	M, 6 months	Right	Diagnosed during life; rapid breathing; dull percussion sound and no breath sounds on right side; heart in right chest
72. Graham and Valle: *J. Thoracic Surg.*, 13: 345, 1944	F, 41 yr.	Left	X-ray showed dense shadow throughout left chest; heart and mediastinum shifted to left; at exploratory thoracotomy only a short bronchial stump with no lung tissue was found on the left side; the right bronchial tree was normal
73. Ibid.	M, 5 yr.	Left	Diagnosis made when child was 9 mo. old; followed for 4 yr. at which time bronchoscopy and bronochograms showed left bronchus to terminate 1 cm. from carina; chest was asymmetric and heart and mediastinum were shifted to left
74. Deweese and Howard: *Radiology*, 42: 389, 1944	M, 6 mo.	Right	Herniation of left lung into right chest; no right main bronchus; heart displaced to right—autopsy finding
75. Ferguson and Neuhauser: *Am. J. Roentgenol.*, 52: 459, 1944	F, 2 yr.	Left	Left bronchus 1 cm. in length; absent left hand; cough since 2 mo.; chest asymmetric; child poorly developed

References	Sex and Age	Side	Findings
76. Ibid.	F, 4 mo.	Right	Small bud-like structure at site of right bronchus; no right pulmonary vessels; patent ductus arteriosus; hypoplasia of spleen
77. Ibid.	M, 6 mo.	Left	Diagnosed in life; left hemithorax smaller than right; left bronchus 3 cm. long; deformed left external ear
78. Ibid.	F, 4 mo.	Right	Diagnosed in life; no right main bronchus; rapid respirations; diminished expansion of left chest; multiple congenital abnormalities of high dorsal vertebrae
79. Ibid.	M, 3 yr.	Left	Diagnosed during life; left chest smaller than right; no left bronchus; hare lip; cleft palate
80. Garber, R. L.: *Am. J. Roentgenol.*, 53: 129, 1945	M, 18 yr.	Left	Diagnosed during life; left chest smaller than right; dull percussion sound and diminished breath sounds on left side; left bronchus 1.5 cm. in length
81. Field, E. C.: *Arch. Dis. Child.*, 21: 61, 1946	F, 1 yr.	Left	Diagnosed during life; left bronchus small blind pouch; spina bifida
82. Ibid.	F, 10 yr.	Left	Diagnosed in life; small rudimentary left lung; asthmatic bronchitis; flattening of left chest
83. Ibid.		Right	Small rudimentary right lung; intraventricular septal defect; cyanosed and coughing since birth
84. Pierson, W. M.: *Ann. Otol., Rhin. & Laryng.*, 35: 604, 1946	M, 5 mo.	Right	No carina or right bronchus; thorax asymmetrical; heart sounds in right chest; dull percussion sounds and absent breath sounds in right chest
85. Widerman and Peters: *J. Pediat.*, 28: 204, 1946	F, 8 mo.	Right	X-ray showed heart displaced to right; barium swallow showed esophagus displaced to right; fusion of 8th and 9th dorsal vertebrae; bronchoscopy showed right bronchus to end blindly
86. Smart, J.: *Quart. J. Med.*, 15: 125, 1946	F, 30 yr.	Right	Chest asymmetric; heart and mediastinum shifted to right; bronchoscopy showed block of right main bronchus
87. Ibid.	F, 29 yr.	Left	Chest asymmetric; heart and mediastinum shifted to left; bronchoscopy and bronchograms showed block of right main bronchus; small trachea
88. Bowden, K. M.: *M. J. Australia*, 1: 646, 1947	F, 15 mo.	Right	No carina or right bronchus; thorax asymmetric; heart sounds in right chest; dull percussion sounds and absent breath sounds in right chest; dyspnea
89. Mollison cited by Wexels.: *Thorax*, 6: 171, 1951	Stillborn	Bilateral	At carina, right and left bronchus ended blindly
90. Burger, R. A.: *Am. J. Dis. Child.*, 72: 481, 1947	F, 2 mo.	Left	Autopsy findings; rudimentary left bronchus; patent ductus arteriosus; patent foramen ovale; two lobes only on right side

References	Sex and Age	Side	Findings
91. Nesbit and Middleton: *Am. J. Roentgenol.*, 57: 446, 1947	F, 50 yr.	Left	Diagnosed during life; small rudimentary left bronchus; slight dyspnea, thoracic tightness and weakness on exertion
92. Yount, F.: *Arizona M. J.*, 5: 48, 1948	M, twin	Right	Dextrocardia; largest twin; deformed right ear; made good progress; spine deformity
93. Ibid.	M, twin	Right	Autopsy performed on this twin who died 36 hours after birth; showed dextrocardia; webbed neck; complete absence of right lung
94. Riddell, R. J.: *M. J. Australia*, 2: 814, 1949	Infant, 1 day	Right	Autopsy findings; heart displaced to right; left lung enlarged and herniated to right; patent ductus arteriosus; very small left pulmonary artery
95. Priest, R. E.: *Ann. Otol., Rhin. & Laryng.*, 59: 889, 1950	F, 4 yr.	Left	Chest asymmetric; heart and mediastinum shifted to left; bronchograms and bronchoscopy showed left bronchus to consist of small blind pouch
96. Ibid.	M, 6 yr.	Left	Chest asymmetric; heart and mediastinum shifted to left; bronchoscopy showed stenosis of left main bronchus
97. Wexels, P.: *Thorax*, 6: 171, 1951	M, 16 mo.	Left	Exploratory thoracotomy; no left lung; no left pulmonary vessels; heart rotated backward and upward to left; patient made uneventful recovery
98. Ibid.	F, 7 yr.	Right	Bronchogram revealed rudimentary right bronchus; bronchoscopy showed very short right bronchus; angiocardiogram showed no patent ductus arteriosus; no patent foramen ovale; physical examination showed right chest flattened; heart displaced to right
99. Brimblecombe, F. S. W.: *Brit. J. Tuberc.*, 45: 7, 1951	F, 3½ mo.	Left	Autopsy findings; no left lung; left pulmonary artery very small; patent foramen ovale; intraventricular septal defect; no left pulmonary vein
100. Ibid.	F, 2 yr.	Left	Diagnosed during life; cyanosis; cardiac murmur, possible patent ductus arteriosus; bronchoscopy showed stenosis of left main bronchus 1 cm. below carina; right cervical rib; 4th and 5th dorsal hemivertebrae
101. Perez, Seiglie, Periera and Hernandez: *Rev. cubana de cardiol.*, 12: 101, 1951	F, 38 yr.	Left	Diagnosis made during life; bronchoscopy showed complete absence of left bronchial tree; angiocardiograms showed absence of left pulmonary artery; superior vena cava displaced to left; heart also displaced to left
102. Barbosa, S. R.: *Clin. Tisiolog.*, 6: 357, 1951	M, 16 yr.	Right	Chest asymmetric; slight dyspnea on exertion; bronchoscopy showed right bronchus to end in blind pouch; diagnosed during life
103. Fouguet, Heimann and Arnoldi: *Bull. et mém. Soc. méd. d. hôp. de Paris*, 67: 1084, 1951	F, 10 yr.	Left	Diagnosed during life; angiocardiogram showed rotation of heart and displacement toward left; superior vena cava and aorta displaced toward left chest wall; left pulmonary artery missing

References	Sex and Age	Side	Findings
104. Thomas and Boyden: *Surgery*, 31: 429, 1952	M, 2 yr.	Right	Patient aspirated foreign body; bronchoscopy for removal was unsuccessful; autopsy showed agenesis of right lung; left lung had three lobes
105. Ibid.	F, twin, 16 days	Right	Died at thoracotomy; tracheoesophageal fistula; right lung absent; left lung had three lobes; autopsy finding
106. Ibid.	M, 1½ hr.	Right	Autopsy findings; agenesis of right lung; left pulmonary artery was posterior to left bronchus; coarctation of the aorta; patent foramen ovale
107. Heege and Hoekstra: *Nederl. tijdscbr. v. geneesk.*, 96: 814, 1952	F, 51 yr.	Left	
108. Rubio and Piovano: *An. Fac. de med. de Montevideo*, vol. 37, 1952	M, 34 yr.	Left	Autopsy findings; left bronchus ended in a small bud of rudimentary lung tissue
109. Ibid.	M, 21 yr	Right	Patient had dyspnea; x-ray showed opaque right chest; thoracotomy showed right bronchus to terminate in small pouch of rudimentary lung tissue; patient made uneventful recovery
110. Macht and Bessinger: *Mt. Sinai Hosp. J.*, 1: 47, 1952	M, 2 days	Left	Tracheoesophageal fistula; thoracotomy performed to repair fistula; died 1 hr. after surgery; left lung absent
111. Putney and Baltzell: *Ann. Otol., Rbin. & Laryng.*, 61: 677, 1952	F, 1 yr.	Left	Diagnosis made during life; slight scoliosis; bronchoscopy and bronchograms showed left bronchus to end in blind pouch
112. Caussade, Neimann, and Beuichoux.: *Arcb franç. pédiat.*, 9: 89, 1952	F, 3 days	Right	Autopsy showed atresia of the esophagus; absence of right lung; tracheoesophageal fistula; coarctation of aorta
113. Maier and Gould: *J. Pediat.*, 43: 38, 1953	F, 10 wk.	Right	Autopsy showed agenesis of right lung; aorta anterior to trachea and compressing it; left pulmonary artery posterior to trachea
114. de Groot and Kwakkelstein: *Maandscbr. v. kindergeneesk.*, 21: 14, 1953	F, 8 yr.	Right	Diagnosis during life; 1 yr. follow-up; chest asymmetric; slight dyspnea; EKG shows some slight cardiac changes; bronchogram showed rudimentary right bronchus; heart sounds in right chest
115. Ibid.	F, 8 yr.	Right	Diagnosis during life; 7 yr. follow-up; chest asymmetric; heart and mediastinum displaced toward right; bronchograms and bronchoscopy showed bronchial tree to end in blind pouch on right
116. Lucas, Dotter and Steinberg: *New England J. Med.*, 249: 107, 1953	M, 22 yr.	Left	Bronchograms showed block of left main bronchus; angiocardiograms showed heart and superior vena cava displaced toward left and also rotated; right pulmonary artery supplying right lung herniated into left chest; patent ductus arteriosus; descending aorta was opacified through the ductus at time of filling of pulmonary artery indicating right to left blood flow; diagnosis made during life

References	Sex and Age	Side	Findings
117. Rey and Rubenstein: *Prensa méd. argent.*, 40: 255, 1953	M, 18 yr.	Right	X-ray showed herniation of left lung into right chest; angiocardiograms showed absence of right pulmonary artery and enlargement of left pulmonary artery; bronchoscopy showed stenosis of right main bronchus
118. Piechaud, Laumonier and Lacoste: *J. de méd. de Bordeaux*, 130: 841, 1953	F, 7 yr.	Left	Left thoracotomy showed large thymus; herniation of right lung into left chest; agenesis of left lung; bronchoscopy showed block of left main bronchus; diagnosed during life
119. da Silva and Chiaverini: *Rev. paulista de med.*, 42: 441, 1953	F, 1 yr.	Right	Chest asymmetric; slight cyanosis on exertion; EKG showed dextrocardia; x-ray and laminograms indicate absence of right lung
120. Bruton, O.: personal communication	F, 3 wk.	Right	Chest asymmetric; cyanosis and dyspnea; autopsy findings: right lung missing; right auricular appendage very enlarged; patent foramen ovale; patent ductus arteriosus; pulmonary veins anterior to the trachea

because after death the large arteries are no longer full and tense.

Esophagography shows the esophagus to be displaced toward the affected side as demonstrated by Wexels, Maier and others.

There are a number of conditions which must be considered in the differential diagnosis of agenesis of the lung. This condition, particularly in the newborn, often resembles atelectasis. It is often impossible to make the diagnosis by x-ray examination alone. Bronchoscopy and bronchography are necessary. Bronchiectasis with atelectasis could simulate agenesis. A postpneumonectomy chest, particularly in a child with an intercostal approach, also could resemble agenesis of the lung. A chest x-ray of a patient with a complete block of one of the main bronchi by a tumor could be mistaken for agenesis. Bronchoscopy, cytologic examination of the bronchoscopic washings or an exploratory thoracotomy will establish the diagnosis. Also fibrothorax should be considered in the differential diagnosis.

From a review of the available data there seems to be no appreciable sex or side linkage in agenesis of the lung. It occurred in ten more females than males and eleven more times on the left than on the right side.

COMMENTS

While it can be said that agenesis of the lung does not preclude a long life as evidenced by its discovery in a seventy-two year old woman (Case No. 35) who died of cerebral hemorrhage and bronchopneumonia, it does diminish the patient's ability to combat serious infections. Many of the persons having this condition die very early in life and the majority before the second decade. Also young patients do not develop so well or so rapidly as normal children do. This is due, no doubt, to the reduced pulmonary function and reserve, and to the fact that this condition is often accompanied by other congenital malformations.

There are various theories regarding the etiology of agenesis of the lung or lungs, but all are agreed that it must occur very early in embryonic life. Also it is apparent that the process of development ceases at varying times since the degree of agenesis varies from complete absence of a main bronchus, through the presence of a rudimentary bronchus to a short bronchus with a small bud of lung tissue.

Arey[1] in his book on "Developmental Anatomy," states that in the developmental anatomy of the bronchopulmonary system, the two bronchial buds arise in the embryo by evagination from the primordial trachea before the end of the fifth week. These primitive lung buds, by progressive branching, eventually give rise to the bronchial tree, from the terminal tubules of which arise small outgrowths which constitute the alveoli. When there is complete absence of a main stem bronchus, therefore, the

anomaly must have had its origin very early in embryonic life. In cases in which the main stem bronchus is either rudimentary or more or less fully formed, the failure of development presumably occurred in a correspondingly later period.

Streeter[3] described the lung buds as first appearing in the human embryo in the period Horizon XIII, i.e., 28 + 1 days after fertilization. In the earlier age group XII, 26 + 1 days, the spot is marked by a ventral bulge of the foregut. Therefore, the agenesis of the lung must take place close to the end of the first lunar month.

Wilson and Warkany[5] noted five instances of agenesis of the left lung in rat fetuses whose mothers had been subjected to a vitamin A deficient diet. The left pulmonary artery was also missing. Many of these rats were found to also have cardiovascular anomalies, such as intraventricular septal defects, poorly developed myocardium and asymmetric development of the aortic arches. Numerous other anomalies were found in the eyes, genitourinary systems, etc. About 75 per cent of the offspring presented some type of deformity. Although Warkany[4] has shown by his experiments that changes in the environment affecting the mother can produce congenital defects in the embryo which have been thought to be hereditary in the past, it cannot be said, at this time, whether genetics or environment play any part in the cause of agenesis of the lung in man.

SUMMARY

A review of 119 cases of agenesis of the lung plus one additional original case is presented. A discussion of the differential diagnosis of this condition and the theories concerning its etiology is also included.

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1. Arey, L. B. Developmental Anatomy, 3rd ed., p. 210. Philadelphia, 1937. W. B. Saunders Co.
2. Schneider, P. In: Schwalbe, E. Die Morphologie der Missbildungen des Menschen und der Tiere, vol. 3, p. 163. Jena, 1913. Gustav Fischer.
3. Streeter, G. L. Age Group XIII, Contributions to Embryology, vol. 31, pp. 30–48. Washington, D. C., 1945. Carnegie Institute.
4. Warkany, J. Congenital anomalies. *Pediatrics*, 7: 607–610, 1951.
5. Wilson, J. G. and Warkany, J. Aortic arch and cardiac anomalies in the offspring of vitamin A deficient rats. *Am. J. Anat.*, 85: 133–155, 1949.

Some Observations on the Function of Pulmonary Structures

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IT is commonplace to refer to the lungs as aeriform structures adapted solely for the purpose of respiration. While this is true in a strict sense, it is known that the lungs are true viscera with entodermal and mesodermal components which react in a physiologic and pharmacologic way as do those structures of the other bodily organs. Nowhere are these reactive phenomena more evident than in the practice of anesthesia. In this field, respiration, that is the uptake of oxygen and elimination of carbon dioxide, is of prime importance. At the same time, one also depends on pulmonic function for the uptake and elimination of anesthetic vapors and gases. But anesthetic agents as well as anesthetic technics may interfere with respiration and the attainment of anesthesia through side effects on the air passages and circulation of blood. As an outstanding example, one needs only to cite intubation of the trachea under a light plane of anesthesia which may produce prolonged coughing, hypertension and tachycardia which persist until the plane of anesthesia is deepened or adaptation to the presence of the tube occurs. Furthermore, some of the anesthetic substances have actions which in turn may lead to bronchospasm and hypotension. In this paper the anatomic stratum on which some of these physiologic and pharmacologic reactions take place will be described.

While the nose and pharynx are parts of the respiratory tract, pulmonary function properly may be said to begin at the larynx. The larynx is a complicated muscular sphincter with the capacity for active constriction and dilation. As Negus[1] has pointed out, the larynx is truly the valve of the respiratory tract. As such it has a commanding role in the protection of the lungs against the entrance of foreign material. However, the production of sound and speech have superseded in importance this original function of the larynx. Less known are those reflex actions which seem to participate in respiration and the responses of the larynx to various types of stimuli applied elsewhere to the body. Direct inspection of the glottis reveals that this aperture widens during inspiration and narrows during expiration. This suggests that the larynx plays a part in respiration perhaps leading to a better distribution of air in the alveoli. Since the laryngeal muscles are innervated solely by the vagi, it is probable that the movements noted are reflex phenomena akin to the Hering-Breuer reflexes which control inspiration and expiration.

It should be apparent, too, that closure of the larynx is needed for the development of positive pressure within the thorax or abdomen. For example, during a cough the glottis first closes to allow for the development of positive intrathoracic pressure. Coincident with contraction of the thoracic muscles the larynx opens and there is enough force released to expel material from the bronchi and trachea. Under adverse circumstances when the larynx remains closed, a greater or prolonged increase in positive thoracic pressure can lead to circulatory collapse by interfering with the return of venous blood to the heart. Although the normal person can compensate for this Valsalva type of action with an increase in sympathetic vascular tone, the anesthetized or "poor-risk" patient may fail to respond in this fashion. Some of the reported instances of cardiac arrest occurring after attempted intubation or extubation of the trachea may have caused by this sequence of events. As a final commentary, the larynx responds reflexly to stimuli applied to other than the respiratory passages. Under light anesthesia closure of the larynx with apnea is one of the commonest reflexes initiated from the operative field. The current practice of using curare to prevent or overcome laryngeal spasm is rational in that

the striated muscles of the larynx are just as susceptible to paralysis as are the other bodily muscles. In summary then, the larynx is really a part of the lungs participating in respiration, in the defense against aspiration, and in the regulation of pressures within the thorax and abdomen.

Beyond the larynx one can proceed logically with a description of the trachea and bronchi. To understand the actions of the conducting portions of the lung, it should be recalled that in the embryo the lungs are an outgrowth of the foregut. Some physiologic and pharmacologic resemblances between the gut and the bronchi still remain in the adult human being. In the process of pulmonary development there is repetitive growth and division of the primary lung bud. According to the anatomic reconstructions of Miller[2] the finest terminal bronchiole changes into a respiratory bronchiole with alveoli in its walls. Successively a respiratory bronchiole leads to alveolar ducts, atria and, finally, alveolar sacs. Important anatomic changes take place at each stage of division. For all practical purposes smooth muscle and cartilage cease to be present beyond the terminal bronchiole. At this point the pulmonary artery, rather than the bronchial artery, supplies blood to the pulmonary tissues for the purpose of respiration. An alveolar duct with its distal communications forms what is known as a primary lobule or the smallest functioning part of the lung. Primary lobules group into secondary lobules, secondary lobules into tertiary lobules and so on until the pulmonary segments are created. There is no denying the pathologic, roentgenologic and surgical importance of the now well defined pulmonary segments, a description of which may be found elsewhere in this series of papers on the lung.

A structure of functional significance in the tracheobronchial passages is the lining epithelium consisting of ciliated columnar cells with mucus-secreting cells interposed. Ciliary action and mucous secretion play a paramount role in the prevention of infection and in the elimination of foreign material. Under proper environmental conditions the cilia under a moist mucus covering flagellate constantly in an oral direction. A practical demonstration of this activity can be seen in a prepared specimen of the hen's trachea[3] in which ciliary action has attained a force of 40 mm. of water. Tenacious plugs of mucus can be propelled and attenuated until the resulting thin mucous films burst. Probably this type of action is one of the chief hindrances to the development of atelectasis in man. For optimum function the cilia must be covered by a moist blanket of mucus. Ciliary action can be impeded by the insufflation of arid gases into the lungs. Likewise cilia can be destroyed by the mechanical action of strong suction from a catheter, by prolonged pressure from an inflated balloon on an endotracheal tube; or cilia can be destroyed chemically by aspiration of gastrointestinal contents into the lungs. Finally, the force of ciliary contraction may be diminished under the influence of narcotics and in the deeper planes of anesthesia. These facts must be remembered in the avoidance of postoperative complications.

Within the walls of the trachea and bronchi as far downward as the terminal bronchioles one finds cartilagenous rings. These serve to maintain the patency of the air passages for in their absence there might be collapse of the airways each time negative pressures were developed in the thorax. Rarely after extirpation of a large goiter or resection of an infiltrating growth in the mediastinum the airways have been known to collapse because of weakening of the cartilages. The cartilages do not completely encircle the walls. This arrangement permits changes in the caliber of the trachea and bronchi which are mediated by the smooth muscles, a part of the lungs which now must be considered.

If one studies properly stained sections of the lung, there is hardly an area without visible smooth muscle.[4] In one sense the lungs are really muscular organs because of this widespread distribution of muscle tissue. The muscle fibers which are interwoven with elastic fibers are arranged in a geodetic manner about the air passages, that is, neither circularly nor longitudinally. With this type of arrangement changes both in length and diameter of the trachea and bronchi can take place during respiration. The manner in which the air passages change in caliber can be seen through a bronchoscope or if one measures the resistance to air flow during inspiration and expiration. During inspiration there is lengthening and dilation of the bronchi while in expiration the reverse changes occur. These rhythmic changes are probably under reflex nervous control and coincide with laryngeal movements. On the

other hand, the muscular movements have been considered to be merely passive in response to changes in intrathoracic pressure.

As suggested above, there is a great similarity between the smooth muscle of the gastrointestinal tract and that of the lungs in the manner of reaction to physiologic and pharmacologic stimulation. In both cases the smooth muscle is capable of spasmodic contraction and peristaltic movement. Spasm of the smooth muscle of the lung may be said to be present temporarily during cough and more persistently during asthmatic crises. In regard to the latter, it is worth noting that the concentration of muscle fibers in relation to the lumen of the bonchus is greatest at the terminal bronchiole. At this point spasmodic smooth muscle contraction can shut off air exchange completely. Bronchial peristaltic movements have been observed during bronchography when the behavior of radio-opaque material has been watched fluoroscopically. The same movements are said to occur in the process of extrusion by cough of any foreign material aspirated into the lungs.[4]

Bronchospasm is a commonly observed phenomenon during anesthesia. It may occur in response to the mechanical stimulation of the airways under light planes of anesthesia in which case cough and laryngospasm are usually an accompaniment. The combined effect of these reflex reactions often produces alarming degrees of anoxia and harmful circulatory responses ranging anywhere from cardiac arrhythmias through hypertension, hypotension and sometimes cardiac arrest. To prevent these phenomena deep planes of anesthesia, topical anesthesia of the mucous membranes or the use of muscle relaxant drugs must be resorted to. In addition to the reactions to mechanical trauma, bronchospasm is seen as a pure pharmacologic response to the inhalation or administration of some of the anesthetic agents. The gas cyclopropane, the intravenous barbiturate thiopental and d-tubecurare which may release histamine after injection, all are agents which can cause constriction of bronchial smooth muscle. On the other hand, diethyl ether, which stimulates the endogenous release of epinephrine is one of the best bronchodilators known, if indeed it does not cause bronchospasm purely in an irritative fashion.

The lungs are the only organs of the body with a double supply of arterial blood and a knowledge of the division of labor between the bronchial and pulmonary arteries is important from the standpoint of understanding respiration and phenomena such as the development of pulmonary edema. Under normal circumstances the bronchial arterial circulation has purely a nutritional function for the tissues of the lung including the tracheal and bronchial walls, the connective tissues, neurogenic elements and the vasa vasorum of the great vessels. This nutritive function explains the anatomic termination of the bronchial arteries at the point of division between the conducting and the respiring elements of the bronchial tree. There are, nevertheless, theoretic aspects of the bronchial circulation which have attracted interest. Since the hydrostatic pressure in the bronchial arteries is that of the systemic arterial circulation, and the bronchial arterial circulation is under neurogenic control, it has been considered possible that the bronchial arteries may play a part in the development of pulmonary edema, especially that of the neurogenic variety. Likewise the fact that part of the bronchial venous blood drains into the pulmonary veins raises the possibility that the bronchial circulation may contribute to the partial oxygenation of systemic arterial blood. Bronchial arterial blood flow has not been measured in man. However, Bruner[5] has estimated the bronchial blood flow in the dog to comprise no more than 1 per cent of the cardiac output, a figure which makes it seem unlikely that bronchial blood flow contributes appreciably to arterial oxygen unsaturation or to the development of pulmonary edema. Under pathologic circumstances the bronchial arteries assume a greater significance. Bleeding from an injured bronchial artery is more apt to be massive and fatal than that from a vessel in the pulmonary arterial circulation. When there is destruction of pulmonic tissue by disease, obstruction to blood flow in the pulmonary artery or a diminished pulmonic blood flow for whatever reason, the bronchial arteries can take over the respiratory function ordinarily held by the pulmonary arteries. Thus in some types of congenital heart disease[6] it is common to find an extensive collateral circulation to the lungs contributed largely by enlarged or accessory bronchial vessels. In bronchiectasis and other suppurative disease of the lungs in which the pulmonary arteries may be thrombosed or destroyed the bronchial arteries again may be

found to have taken over the circulatory part of respiration.

The role of the pulmonary arteries in respiration is quite apparent yet attention must be paid to the manner of regulation of pulmonary arterial blood flow. Unlike the bronchial arteries the tone of pulmonary arterial vessels seem to be relatively free of neurogenic influence. In this respect the pulmonary arterial circulation resembles that to the brain and heart in which the vessels are responsive more to the partial pressures of oxygen and carbon dioxide in the circulating blood. In all three instances a decrease in arterial oxygen saturation produces a purposeful vasodilation while full oxygen saturation produces a relative vascular constriction. Likewise, an increase in circulating carbon dioxide creates vasodilation and a decrease in carbon dioxide tension results in vasoconstriction. Vital as is the circulation to the lungs, heart and brain, it is fortunate that the regulating mechanisms seem to be adjusted to the metabolic demands of the tissues involved. The circulation to somatic tissues may be said to be regulated grossly by the nervous system while that to the vital organs is under a finer type of control. In the case of the pulmonary arteries, an additional method for regulating blood flow has been shown to exist in the partial pressures of oxygen and carbon dioxide in the alveoli.[7] Thus low oxygen tensions in the alveoli lead to vasoconstriction which is the opposite to what might be expected. Nevertheless, it is another instance of what may be termed a purposeful regulation in that the pulmonary blood flow to alveoli is shunted toward well ventilated areas of the lung. This probably accounts for the relatively minor degree of arterial oxygen unsaturation in the presence of conditions such as atelectasis.

It is remarkable that the lungs remain free of fluid accumulation since their aeriform structure offers little resistance to the passage outward of fluid from the capillaries. Several factors account for this freedom from edema. In the first place the lungs are supplied extensively with lymphatics which drain off tissue juices as soon as they accumulate.[8] Secondly, hydrostatic pressure in the pulmonary arterial capillaries, or the outward driving force as far as fluid is concerned, is far less than that in the systemic circulation. Mean pressures in the pulmonary capillaries must be less than the mean pressure in the pulmonary artery which, on the average, attains no more than 18 mm. of mercury in normals. The osmotic action of protein in the circulating blood which draws fluids from the tissues far exceeds the outward driving force in the pulmonary capillaries. When there is pulmonary arterial hypertension, the chance for the development of pulmonary edema is naturally greater.

In the discussion of the bronchial arterial circulation reference was made to the development of a collateral circulation of blood in response to pulmonary disease conditions. Still another type of collateral circulation exists in the lungs and that is the collateral circulation of air between segments of the lungs which occurs apparently under normal conditions. It would not have been supposed in view of the mode of development of the lungs that there could be communicating pores between the alveoli peripherally. Always when demonstrated microscopically such communications were assumed to be artifacts. Yet in investigating the factors leading to the onset of atelectasis Van Allen et al.[9] found that occlusion of a secondary bronchus did not lead to atelectasis. Subsequent investigation revealed that there was collateral transfer of air from adjacent tissues to those presumably denied ventilation. This phenomenon has been proved to be present in man and the peak volume of collateral ventilation has been estimated to reach 40 per cent of the expected normal ventilation.[10] The significance of collateral ventilation is great from the standpoint of prevention of atelectasis and infection. Probably a good many of the measures which are directed toward the prevention of postoperative pulmonary complications serve to maintain collateral respiration at effective levels.

In the preceding discourse many references were made to neurogenic action and to reflex activity taking place in the lungs. This presupposes the presence of a visceral nerve supply which the lungs do have. Like that to other viscera the nervous supply comes from the autonomic nervous system with representation both from the sympathetic and parasympathetic portions. Yet the functions of these nervous elements have not been established clearly chiefly because of difficulties in anatomic dissection, inability to apply the result of animal experiments to man, and the final fact that the nerve supply to the heart is almost identical to that of the lungs. The reaction of the tissues

of the lung in asthma, the responses in atelectasis and pulmonary embolization, the problem of pulmonary pain and the recent exposition of the presence of pulmonary chemoreceptors all have focused attention on the nerve supply to the lungs. Attempts to treat asthma by surgical means have failed for a variety of reasons. It is evident that asthma is not a disease entity *per se* but actually a reaction of bronchial smooth muscle to a variety of excitants. Further, if the lungs have been denervated extensively, the smooth muscle still can react to direct excitation or through intrinsic nervous reflex arcs. However, attempts to treat asthma surgically have clarified some of the afferent nervous pathways from the lungs particularly those carrying pain.[11] It now appears that afferent fibers carrying the sensation of pain and those mediating the cough reflex both travel with the vagi. Thus it now may be possible by surgical means to relieve pain arising from inoperable disease in the lungs.

SUMMARY

This discourse has concerned itself with some of the functions of pulmonary tissues other than those related directly to respiration. It was pointed out that the lungs contain anatomic structures which react in a characteristic manner to mechanical, pharmacologic and physiologic stimuli. Thus the so-called functional anatomy of the larynx, tracheobronchial tree, the blood supply and innervation of the lungs were presented. Reference was made to reactive phenomena which occur frequently during anesthesia and to reactions of pulmonic tissues in the prevention of infection.

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Physiology of Respiration with Reference to Pulmonary Disease

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THE essential features of respiration are related to the maintenance of normal tissue oxygen tension and to the adequate removal of carbon dioxide at all times. The adequacy of the blood gas exchange can be studied during both rest and exercise from measurements on lung volumes, arterial blood and the expired air. One set of measurements provides information on the bellows action of the chest and lungs regarding the ability of the individual to move air in and out of the lungs in adequate volumes. The other set of measurements provides information on the blood gas exchange regarding the transport of oxygen and carbon dioxide across the lungs to the blood. A battery of test measurements are necessary to provide accurate information on the extent and type of disturbed function in the individual case regardless of the etiology. No single test is satisfactory for the accurate and complete clinical evaluation of the extent of pulmonary function impairment.

Oxygen may be administered by several methods providing a normal arterial blood saturation, but a saturation of 96 per cent or more does not insure an adequate removal of carbon dioxide, if (1) alveolar aeration be inadequate either because of a pulmonary minute ventilation too small or a tidal air volume too shallow, or (2) to perfusion of blood through poorly or non-ventilated alveoli of the lungs. When the respiratory gas exchange is inadequate and treatment is required, the two main factors to be considered are (1) an inspired oxygen partial pressure (pO_2) of sufficient magnitude to saturate the arterial blood to the normal level of 96 to 98 per cent and (2) an adequate minute ventilation to provide a sufficiently uniform alveolar aeration to blow off the carbon dioxide.

LUNG VOLUME MEASUREMENTS

Information regarding the efficiency of the chest and lungs as a bellows may be obtained from spirogram tracings and from the residual air capacity measurement.[1] The total vital capacity, the timed vital capacity for three seconds, and the maximal breathing capacity are obtained from rapid spirogram tracings on the 13½ L. respirometer.* Total vital capacity is obtained both in the supine and standing positions. A marked reduction in the total vital capacity in the standing position as compared to the supine position indicates the presence of severe pulmonary insufficiency. The timed vital capacity for three seconds in the standing position is obtained by having the patient take in as deep a breath as possible, hold the breath momentarily and then on command blow the air out of the lungs as rapidly as possible. The volume exhaled in the first three seconds from the exact beginning of expiration is called the three-second timed vital capacity. The timed vital capacity for three seconds is normally the same as the predicted total vital capacity. The timed vital capacity for three seconds is an important measurement of vital capacity, as this is the maximal effective portion which can be used with a respiratory rate of 15 or more per minute (a rate of 15 per minute requires four seconds per breath and one second is allowed to breathe in). Vital capacity is commonly measured by having the individual take a deep breath and then blow out all of the air as far as possible. Vital capacity may be taken, however, by having the individual first blow the air out of the lungs as far as possible and then take in as deep a breath as possible. In the normal individual there is no significant difference between the two methods, but in some patients with pulmonary disease a better vital capacity measurement may be obtained

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by the second method. In either procedure the volume difference is measured between maximal inflation and maximal deflation of the lung, and no good clinical evidence exists that measuring the volume difference between maximal deflation followed by maximal inflation is not just as valid. The level of the diaphragm may shift with position and activity. The measurement of vital capacity in separate steps (the sum of inspiratory reserve and expiratory reserve) is subject to error with shifts in the level of the diaphragm and is unsatisfactory.

The maximal breathing capacity (MBC) reveals the largest volume of air which an individual is able to move in and out of the lungs in a given short unit of time (twelve to fifteen seconds) but is expressed as L. per minute. The individual is instructed to breathe as deeply and as rapidly as possible for twelve seconds (never longer than fifteen seconds), and the rate and depth varied in successive trials (not less than three) to obtain the maximal value. The 13½ L. respirometer was developed to provide a mechanical recorder with minimal breathing resistance for deep, fast breathing and to permit quick accurate determinations of the MBC value (five to ten minutes).[2] When the rate and depth of breathing are properly varied, one obtains the greatest MBC of which the subject is capable and the learning factor as such is not a significant feature. The degree of bronchospasm is measured quantitatively by comparing the MBC before and immediately after one bronchodilator treatment.

In men a maximal breathing capacity of 120 L. per minute indicates no significant degree of pulmonary emphysema present, if the maximal breathing capacity is less than 40 L. per minute the presence of a significant degree of emphysema is indicated.[3] A maximal breathing capacity between 40 and 120 L. per minute is indeterminate with respect to the presence or absence of a significant degree of pulmonary emphysema. The spirogram tracings in emphysema characteristically reveal prolonged exhalation time, evidence of air trapping after a few deep breaths in rapid succession as during the maximal breathing capacity test involving rapid voluntary respiratory movements, the lungs are kept filled with more air than normal (high inspiratory level) which elevates the tracing of the rate and depth of breathing on the record and indicates increased breathing resistance.

The shape of the spirogram tracings as observed on the rapidly moving kymograph drum (32 mm. in twelve seconds) reveals characteristic features of the expiratory flow. The slow prolonged exhalation curve indicates obstruction to the air flow, and the failure of the exhalation curve on the tracing to return to the beginning level indicates air trapping. Satisfactory spirogram tracings can be obtained usually in five to ten minutes, a slightly longer time period is required to evaluate the degree of bronchospasm, since the bronchodilator should be administered over a period of at least ten minutes. Measurements obtained from spirogram tracings are useful: in evaluating the response to treatment, in following the clinical course of a disease by obtaining serial spirogram tracings at intervals, in screening tests for surgery, in detecting anesthetic risks, in eliminating poor risks in workers exposed to lung irritants and environmental dust hazards and in providing information on other types of problem cases. Spirogram tracings represent simple pulmonary function tests that provide a tremendous amount of information of the status of an individuals lungs.[2] Normal spirogram tracings of the three-second timed vital capacity and the maximal breathing capacity indicate the presence of normal lung elasticity, the absence of obstruction, good movement of the diaphragm and the absence of a significant degree of pulmonary emphysema.

The residual air normally occupies about 25 per cent of total lung capacity being slightly less in the younger age group (20 per cent for adults under thirty-five years of age) and slightly more for individuals over sixty years of age (30 per cent). Data obtained in this laboratory from studies on 100 patients with normal spirogram tracings (including the total vital capacity, the timed vital capacity for three seconds, the maximal breathing capacity and the shape of the exhalation curve) with an age range of sixteen to seventy years indicate that the increase in residual air capacity is of small magnitude even with the aging process and normally does not exceed 35 per cent of total lung capacity.[4] It is realized that many individuals have residual air volumes which represent more than 35 per cent of total lung capacity who are still working

and report no pulmonary complaints, but this does not mean that their lung volumes are normal any more than a blood pressure of 210/140 is considered normal even though the patient has no complaints and may work for many years with the elevated pressure. There is a very large breathing reserve in a normal lung as attested by the fact that many individuals with one good lung can get along remarkably well following a pneumonectomy.

Residual air capacity can be accurately measured using the oxygen open circuit method[1,5] allowing the patient to breathe 100 per cent oxygen for seven minutes with collection of all the expired air during the breathing period in a large gasometer. If the alveolar air sample contains more than 1.5 per cent nitrogen after breathing oxygen for seven minutes, impairment in the uniformity of air distribution in the lung exists. Small samples of the air in the gasometer are analyzed for the per cent of nitrogen, and the total volume of nitrogen washed out during the seven-minute period of breathing is computed from the total measured volume and the sample analysis. The volume of air in the lungs required to contain the volume of nitrogen washed out can then be calculated, after making suitable corrections for the nitrogen diffusing from the blood during the seven-minute period of oxygen breathing. The residual air capacity plus the vital capacity equal total observed lung capacity (TLC) for the individual case, and in pulmonary emphysema the TLC value may be the normal predicted, increased or decreased. Wide individual variations have been noted for the total lung capacity in patients with pulmonary emphysema,[6] for in some cases the total lung capacity may be increased as much as 40 per cent above the normal predicted and in other cases decreased more than 50 per cent below the normal predicted. The total lung capacity may be normal, increased or decreased in an individual case, hence the ratio of the residual air to total lung capacity is most important, as this corrects for changes in total lung volume and permits proper evaluation of the degree of the pulmonary emphysema. Pulmonary emphysema has been classified on a quantitative basis by expressing the residual air as the per cent of total lung capacity. If the residual air occupies less than 35 per cent and more than 25 per cent of total lung capacity, a slight but insignificant degree of pulmonary emphysema may exist. If the residual air occupies 35 to 45 per cent of total lung capacity a moderate, but significant degree of pulmonary emphysema exists, from 45 to 55 per cent an advanced or severe degree of pulmonary emphysema exists, and above 55 per cent a far advanced or very severe degree of pulmonary emphysema exists. In some cases the degree of pulmonary emphysema present as determined by the physiologic method was very poorly correlated with the x-ray films and even the physical examination was misleading. Accurate residual air measurements remove the uncertainty of the evaluation of the amount of emphysema present and provide information valuable in clinical management of the individual case.[6]

A numerical ventilation factor (V.F.) has been used to evaluate the efficiency of the chest and lungs as a bellows from the average of (1) the timed vital capacity for three seconds, (2) the maximal breathing capacity and (3) the residual per cent of total lung capacity, all three expressed as per cent of the normal predicted on a basis of 100 per cent for the normal.[1] The ventilation factor provides a single figure value of the patients ability to use the chest and lungs as a bellows for aerating the alveoli and this figure has been found to be well correlated with the arterial pCO_2 by direct tension measurement[2] and the inspired-alveolar pO_2 difference in mm. Hg[6] calculated by direct tension measurements of arterial pO_2 and pCO_2 and the expired air pCO_2. If the ventilation factor is decreased as low as 25 per cent of the normal predicted, dyspnea is usually present at rest. A low ventilation factor indicates a poor anesthetic risk.

In general, when respiratory complaints are present in pulmonary emphysema the pathological changes responsible are very extensive. The large pulmonary reserve in man often obscures clinical or roentgenologic detection in the presence of severe emphysema, obvious clinical symptoms being a late manifestation as so often is found in pulmonary fibrosis and emphysema.

Newer research technics of promise providing information on the status of air flow in the lung include pulmonary compliance tests as described by Mead and associates.[7] Pulmonary compliance on the distensibility of the lung is obtained from recording of two variables (lung volume and intrapleural pres-

sure from the esophagus) simultaneously on an oscilloscope in the form of a loop, and the volume determination is divided by the pressure determination to get the compliance value (normal 150 to 250 ml. per cm. water pressure). The use of the nitrogen meter[8] for obtaining nitrogen exhalation curves appears very promising, but as yet more studies are needed regarding the practicability and reliability of both test and apparatus.

OXYGEN TRANSPORT IN THE LUNG

The direct determination of the oxygen tension[9] (pO_2) and carbon dioxide tension (pCO_2) in the arterial blood has been most helpful in studying the transport of oxygen across the lung to the blood.[10] The difference between the mean oxygen partial pressure (pO_2) of inspired air (150 mm. Hg at sea level) and that of the alveolus is referred to as the aeration gradient (normal 50 mm. Hg) and the difference between the mean oxygen partial pressure of the alveolus and that of the arterial blood is designated as the transfer gradient (normal 5 mm. Hg). Elevation of the transfer gradient indicates changes in the alveolar-arterial oxygen gradient from all causes including: diffusion defect with increased resistance in the pulmonary membrane, shunting of blood through non-ventilated areas and impaired alveolar aeration and perfusion. Factors interfering with the oxygen respiratory gas exchange are primarily those related to mixing and dilution, diffusion, shunting and distribution.

Decreased ventilation (reduction in vital capacity, maximal breathing capacity, the timed vital capacity single or combined), increased residual air or increased ratio of residual air to total lung capacity (pulmonary emphysema), impaired diffusion, shunting and poor distribution are the factors most often responsible for the lowering of the arterial blood oxygen saturation. Normally there is a predictable relationship between the arterial pO_2 and the per cent saturation as given by standard charts showing the blood oxygen hemoglobin dissociation curve in relation to the pH. However, in chronic pulmonary disease in which there is venous admixture or areas of the lung perfused but not ventilated this ratio may no longer hold as blood by-passes the ventilated areas and blood gas exchange occurs only with the blood which comes in contact with the alveoli. Thus where there is venous admixture or shunting of a sufficient degree, the arterial blood oxygen saturation will not be 100 per cent saturated even on oxygen breathing and in the presence of a quite high arterial blood pO_2 tension. In order for all of the blood to be saturated (all hemoglobin combined as oxyhemoglobin), intimate contact with the red blood cell and the alveolar gas is required, as the red cells normally pass through the capillaries of the lung in single file. There are normally 4 to 5 million red blood cells per cu. mm. and with a total blood volume of about 5 L., many million red blood cells must come in close contact with the alveolar gas in the lung capillaries so that all of the hemoglobin may be combined as oxyhemoglobin and thus provide 100 per cent saturation. When a significant degree of venous admixture is present (perfusion without ventilation), unsaturation results even though the oxygen tensions be quite high in arterial blood as a result of exposure of ventilated alveoli to high oxygen tension. A high oxygen tension in the blood does not insure complete saturation of all the red blood cells because there is not an adequate opportunity for the intimate contact required to insure that all of the hemoglobin will be combined with oxygen to form oxyhemoglobin.

The aeration gradient (the difference between the inspired pO_2 and the mean alveolar pO_2) is increased by a high residual air volume, hypoventilation, retained secretions impairing alveolar aeration and bronchospasm with a resulting lowering of the alveolar pO_2 and in turn the arterial blood oxygen saturation. Hyperventilation may lower an elevated aeration gradient to normal and decrease the alveolar pCO_2. Increased resistance for the movement of oxygen across the pulmonary membrane constitutes a true diffusion difficulty and lowers the arterial pO_2 and the oxygen saturation. Changes in the pulmonary membrane affecting oxygen diffusion are independent of pulmonary emphysema which may or may not be present.

Most venous admixtures of a severe degree occur in congenital cardiac anomalies and arteriovenous fistulas[11] of the lung with very high mean gradients of pressure between the alveoli and arterial blood (transfer) also seen in the presence of diffusion difficulties as beryllosis. Unequal alveolar aeration and perfusion (the distribution factor) constitutes a common

cause of the elevation of the transfer gradient in chronic pulmonary disease, being by far the most common factor.[6] Fibrosis produces various degrees of impairment of air circulation to the alveoli (there is a loss of lung elasticity and a narrowing of the bronchioles) so that although perfusion may be present for some alveoli, ventilation may be inadequate or absent. Alveoli which are perfused but not aerated represent circulatory pathways which are small shunts[12] and lower the arterial blood oxygen saturation so that if there is a generalized disturbance of this nature shunting of a marked degree may occur. The blood flow to alveolar capillaries may be obliterated to a greater or lesser extent, resulting in ventilation without perfusion and the alveoli so involved are functional dead space. Hyperventilation can improve the oxygen transfer only in those alveoli that are poorly ventilated but still perfused with blood. The distribution factor is commonly involved in such chronic pulmonary conditions as fibrosis and emphysema and may be present in various degrees where there is obstruction to alveolar aeration as in atelectasis, consolidation of the lungs, retained secretions or fluids and bronchospasm.[12]

The normal movement of the diaphragm with the intercostal muscles provides a bellows to pump air in and out of the lungs in sufficient quantities to supply the necessary amount of oxygen and to remove effectively the carbon dioxide produced by metabolic processes. In the normal individual this bellows-like action of respiration provides a fairly uniform alveolar aeration, although usually a small number of alveoli are more fully aerated than the others (that is, a small percentage of the alveoli are relatively hyperventilated and a small percentage hypoventilated). However, the preponderance of the alveoli are normally ventilated thus providing an adequate oxygen intake and carbon dioxide output even though the cardiac output may be increased three times or more with exercise. Impairment of the bellows action of the chest and lungs because of pathologic changes may severely alter the blood gas exchange as a result of defective alveolar aeration. Impairment of the function of efferent nerves from the respiratory center to the respiratory muscles, loss of lung elasticity by fibrosis, narrowing of the bronchioles by fibrosis, spasm or secretion, emphysema or chest deformities are factors interfering with the normal use of the chest and lungs as a bellows.

Measurements on arterial blood are obtained both at rest and immediately after one minute of step-up exercise (thirty steps on an 8-inch stool). A drop in the arterial blood oxygen saturation of 5 to 10 per cent or more below the resting level with mild exercise indicates severe disability. An increase in the exercise oxygen saturation above the resting level indicates less disability than implied by the resting level measurement. In general, the exercise saturation tends to decrease in severe emphysema, but this is not always the case; and in pulmonary fibrosis without emphysema a marked drop in exercise arterial blood oxygen saturation frequently occurs. The saturation of the blood perfusing the lung during exercise may not be decreased even though the oxygen uptake is markedly decreased and this indicates the inability to increase the pulmonary blood flow adequately during the exercise, proportionate to the test, although the blood that gets through comes in contact with aerated alveoli and may be normally saturated. In some cases of emphysema the hyperventilation (as measured by the minute ventilation volume) may be adequate to maintain the normal sea level difference in providing a mean alveolar pO_2 of 100 mm. Hg. The mean inspired-alveolar pO_2 difference correlates well with the ventilation factor in a large series of cases.[6] Intermittent positive pressure breathing (IPPB) with compressed air[10] restores the arterial blood saturation to normal or near normal in many cases of emphysema by improving the ventilation in the poorly aerated alveoli as compared to the ambient breathing, and constitutes a valuable test as to the cause of the unsaturation. Shunting of blood through non-ventilated areas results in arterial oxygen unsaturation which cannot be improved by the ventilatory approach, with IPPB and even on 100 per cent oxygen breathing the arterial blood is not 100 per cent saturated. In some cases the drop in the exercise saturation as compared to the resting results from inadequate alveolar aeration, and this can be demonstrated by performing the step-up exercise using IPPB on compressed air to increase alveolar aeration. If the exercise drop is due to increased resistance in the alveolar-capillary membrane, the IPPB will have no effect, but breathing 30 per cent oxygen in nitrogen during

the exercise should give a normal saturation. If a shunt exists the blood will be unsaturated during exercise on the high oxygen breathing mixture, even after breathing 100 per cent oxygen. The above tests provide information as to the nature of the arterial blood oxygen unsaturation.

REGULATION OF CARBON DIOXIDE IN THE BODY

Information on the status of carbon dioxide is obtained from actual measurements of the minute ventilation in L. per minute, respiratory rate, tidal volume, the arterial blood pH direct on a glass electrode, the arterial CO_2 content, the CO_2 combining power and the direct tension measurement of arterial pCO_2. The direct measurement of the arterial blood pH on a glass electrode apparatus is the most practical single test to provide quickly accurate information concerning the exact status of acidosis or alkalosis and this also serves as a very useful guide in regulating treatment procedures in either acidosis or alkalosis. The CO_2 combining power and even the arterial CO_2 content cannot be relied upon in many cases of chronic pulmonary disease especially with emphysema because of wide individual variations observed when correlated with direct measurements of the arterial blood pH. Numerous published reports emphasize the importance of evaluating the status of carbon dioxide to prevent the development of respiratory acidosis as in prolonged surgical procedures especially chest operations even in the presence of a normal arterial blood oxygen saturation provided by an anesthesia machine with oxygen but with an inadequate alveolar ventilation to blow off the CO_2.

An elevated arterial CO_2 content (normal 48.5 volumes per cent at sea level) indicates impaired alveolar aeration and warns of the possibility of respiratory acidosis developing during infections or a depressed respiration by sedative drugs, anesthetics, high oxygen breathing or by any other means. Drowsiness, stupor or coma, characteristic symptoms in respiratory acidosis, appears to be related to pH changes rather than the absolute level of the CO_2 content or pCO_2. The mental status correlated with arterial blood studies over a twelve-week period in a patient with a very severe degree of pulmonary insufficiency complicated by infection was related to pH changes rather than the absolute level of the CO_2 content or pCO_2. Patients with chronic pulmonary disease and an advanced degree of pulmonary function impairment with hypoxemia may occasionally become drowsy, stuporous, delirious, unconscious, and even die from respiratory acidosis when subjected to high concentrations of oxygen by catheter, mask or tent, a phenomenon attributable to the development of a high pCO_2 and a low pH from a depressed respiration previously being maintained primarily reflexively from the carotid bodies by the hypoxic stimulation. The respiratory center apparently becomes tolerant to increased carbon dioxide so the latter has no further stimulating effect. In such a patient a sudden change to high oxygen breathing decreases the minute ventilation by removing part of the reflex stimulation of the respiration center from the carotid bodies which are stimulated by the low oxygen saturation of the blood. The high oxygen breathing relieves the arterial blood oxygen unsaturation and removes the stimulus from the carotid bodies and the total minute ventilation decreases, in some cases to a critical level unless supported by mechanical aids as IPPB. The data given in Table 1 reveal the rapid onset of respiratory acidosis, which can be demonstrated in some cases of severe pulmonary emphysema even after short (six-minute) periods of high oxygen breathing as measured by changes in the pH and CO_2 content. However, as previously pointed out the direct determination of the arterial blood pH reveals the exact status of the acidosis or alkalosis at the time regardless of what the oxygen or CO_2 content, pCO_2 or CO_2 combining power may be.

An increase in carbon dioxide tension of the blood normally constitutes a strong stimulus to the respiratory center, primarily by direct action, with a resulting increase in pulmonary ventilation (such as seen normally when a mixture of 5 per cent CO_2 with air or oxygen is breathed for a short interval). Other afferent impulses which stimulate the respiratory center reflexively and increase pulmonary ventilation are: the Hering-Breuer reflex from the lung alveoli, low blood oxygen saturation with stimulation of carotid and aortic bodies, painful stimulation of peripheral nerves, changes in the systemic blood pressure and the influence of higher cerebral centers. The rate and depth of breathing and the minute ventilation volume represent the resultant of

all reflexes and direct stimuli acting on the respiratory center. The normal function of the respiratory center depends on an adequate oxygen supply; and if the oxygen lack be severe enough, the respiratory center will fail completely. The respiratory center tends to acquire or develop tolerance with a lowered sensitivity to changes which develop slowly as a decreasing pO_2 and an increasing pCO_2, commonly present in chronic pulmonary insufficiency. If the fall in the blood oxygen tension occurs slowly, very low levels may frequently be reached with little direct stimulating effect on the respiratory center; also a similar mechanism applies in reverse for carbon dioxide, which may gradually increase in the blood to a level at which the respiratory center becomes refractory to concentrations that were formerly effective. However, in severe hypoxemia if the oxygen saturation in the arterial blood be suddenly lowered and the drop be of sufficient magnitude or if the carbon dioxide tension of the blood be elevated markedly an increase in respiration or minute ventilation may occur although the sensitivity of the response is markedly reduced in relation to the magnitude of the stimulus normally effective.

TABLE 1

MEASUREMENTS OF ARTERIAL BLOOD OXYGEN SATURATION, CARBON DIOXIDE CONTENT AND PH ON AIR AND AFTER SIX MINUTES OF 99.4 PER CENT OXYGEN BREATHING IN TEN PATIENTS WITH SEVERE PULMONARY EMPHYSEMA AND HYPOXEMIA*

Case	Residual Air, Per cent of Total Lung Capacity	Air Breathing			Oxygen Breathing, Six Minutes		
		O_2 Saturation %	CO_2 Content, Volumes %	pH	O_2 Saturation %	CO_2 Content, Volumes %	pH
1	52.8	85.3	63.1	7.50	94.5	64.9	7.44
2	54.9	90.0	49.6	7.46	100.0	49.8	7.43
3	50.8	91.3	51.1	7.52	98.8	51.3	7.45
4	66.6	66.2	68.5	7.33	100.0	68.9	7.23
5	61.5	87.8	49.1	7.41	100.0	49.9	7.35
6	56.2	85.0	41.8	7.58	91.0	43.0	7.37
7	59.8	83.8	49.2	7.46	99.8	52.1	7.35
8	59.2	62.3	63.7	7.37	100.0	65.1	7.29
9	62.1	87.3	55.3	7.45	97.4	56.5	7.37
10	59.4	92.6	50.6	7.45	98.8	51.2	7.42

* Oxygen saturation based on arterial oxygen content and capacity on Van Slyke and cuvette double scale Waters-Conley oximeter, CO_2 content on Van Slyke and pH on Cambridge glass electrode. Note the greater degree of respiratory acidosis present in the most severe cases of hypoxemia during oxygen breathing.

Patients needing artificial respiration to supplement ambient breathing already have an elevated arterial blood pCO_2 so that the further use of carbon dioxide in oxygen (as 5 or 7 per cent) is not physiologic.[12] The use of 5 per cent carbon dioxide would only increase the acidosis of the subject in need of artificial respiration. Studies of arterial blood before treatment in patients needing artificial respiration reveal decreased oxygen tensions, arterial oxygen unsaturation, increased carbon dioxide content, increased pCO_2 and decreased arterial blood pH. It is a popular misconception that carbon dioxide mixtures are valuable in the treatment of respiratory depression or asphyxia. Mixtures of carbon dioxide as high as 25 per cent have been advocated for use in artificial respiration on the assumption that a respiratory center too depressed to respond to 5 per cent carbon dioxide would respond to a higher concentration. In the asphyxiated patients the blood carbon dioxide level is above normal so that the carbon dioxide no longer acts as a respiratory stimulus; in fact, it may be a depressant. In dogs subjected to experimental severe acute hypoxia 5 per cent carbon dioxide produced respiratory depression, and 15 per cent carbon dioxide produced even more profound respiratory and circulatory depression when administered in the same stages of hypoxia.[13]

Adequate removal of carbon dioxide depends on the minute ventilation and the uniformity of alveolar aeration and perfusion. If the respiration is depressed, the carbon dioxide increases and the pH of the arterial blood decreases (respiratory acidosis). Present concepts indicate that there is no rational basis for the use of carbon dioxide in asphyxia and that such a procedure is not only contraindicated but dangerous. Recently an experimental study was reported indicating that even in carbon monoxide poisoning, the addition of CO_2 to oxygen does not appear advantageous, oxygen alone being preferable.[14] The Council of Physical Medicine and Rehabilitation of the American Medical Associa-

tion and the American Red Cross now recommend that oxygen alone be used in resuscitators or inhalators instead of a mixture of oxygen and carbon dioxide.

ACID-BASE BALANCE

The maintenance of a normal acid-base balance depends principally on the buffer system of the blood and the respiratory segment of the acid-base balance, although quite narrow normally responds rapidly to correct for sudden changes in CO_2. The ratio of $\frac{H_2CO_3}{BHCO_3}$ in the blood in the bicarbonate system is normally 1:20. The concentration of carbonic acid in the arterial blood can be rapidly decreased by hyperventilation increasing alveolar aeration and lowering alveolar pCO_2 and in turn the arterial pCO_2 which is practically the same as the alveolar pCO_2. The blowing off of carbon dioxide from the lungs tends to restore the normal ratio of $\frac{H_2CO_3}{BHCO_3}$ (1:20) and a normal pH when the carbonic acid is increased by fixed acids, a reaction which occurs much more rapidly than can be accomplished by the excretion of acid in the kidneys. The pH is not dependent on the total carbonate or alkali reserve (a term used to designate the total quantity of carbon dioxide in the plasma bound as bicarbonate). The ratio of $\frac{H_2CO_3}{BHCO_3}$ may be 1:20, but the quantity of each could be three times the normal value (3:60 with a ratio of still 1:20 and a normal pH). The volume of carbon dioxide combined at 40 mm. Hg in the plasma is the carbon dioxide combining power (commonly used clinically as the measure of the available alkali); however, this measurement does not provide directly the concentration of either total carbon dioxide or bicarbonate in the blood, hence the shortcomings of this measurement in many cases of chronic pulmonary disease of long standing. The pCO_2 of the arterial blood is a function of alveolar aeration and responds quickly to changes in pulmonary ventilation and in the presence of a normal buffer base an abnormal bicarbonate content may result. Alterations in the acid-base balance are common in chronic pulmonary disease and such disturbances may involve shifts in the blood buffer base and pCO_2 in opposite directions with variable pH values so that in a given case the only way to be certain of the pH is the direct measurements on arterial blood using a glass electrode. A poor correlation of the arterial CO_2 content and the pCO_2 with the pH has been observed by direct measurements of these values in cases of severe pulmonary insufficiency, in which with an arterial blood pH range of 7.40 to 7.46 the CO_2 content varied from 42 to 62 volumes per cent and the pCO_2 from 27

TABLE II

MEASUREMENTS* ON ARTERIAL BLOOD AT REST AND THE VENTILATION FACTOR IN THIRTY CASES OF SEVERE PULMONARY INSUFFICIENCY

Case No.	pH	CO_2 Content (vol. %)	pCO_2 (mm. Hg)	O_2 Saturation (%)	Ventilation Factor (%)
1	7.48	50.3	45.6	89.8	38.6
2	7.49	45.4	32.4	91.9	38.7
3	7.41	55.7	56.7	74.6	30.7
4	7.43	45.5	33.6	92.2	38.8
5	7.48	44.9	39.4	85.5	34.9
6	7.49	61.3	40.7	91.8	32.8
7	7.47	54.9	44.0	90.2	45.9
8	7.43	62.3	55.0	82.0	29.7
9	7.51	49.4	34.7	93.7	35.0
10	7.47	58.7	36.5	94.6	32.3
11	7.49	54.0	45.5	90.4	39.8
12	7.46	46.8	42.8	84.9	42.8
13	7.45	53.7	47.0	87.5	33.8
14	7.47	54.1	42.1	89.1	34.2
15	7.42	51.8	49.4	90.9	24.0
16	7.47	52.8	40.6	93.0	36.0
17	7.44	42.3	27.4	91.9	37.0
18	7.55	49.7	46.5	91.6	37.8
19	7.41	60.2	55.0	86.7	27.5
20	7.45	45.5	47.4	86.0	41.8
21	7.46	45.6	46.0	93.0	21.6
22	7.44	56.1	53.8	82.1	32.8
23	7.45	48.4	46.2	92.0	40.7
24	7.38	52.0	53.5	85.4	39.4
25	7.33	68.5	72.0	66.2	23.0
26	7.41	49.1	40.7	87.8	31.5
27	7.58	41.8	47.1	85.0	39.6
28	7.43	44.6	44.1	91.6	41.4
29	7.46	49.2	61.1	83.8	28.9
30	7.37	63.7	64.0	62.3	26.8

* pH. Glass electrode direct; CO_2 Cont., Van Slyke manometric; pCO_2 direct tension measurement (Riley bubble method); O_2 saturation from Van Slyke content and capacity. Ventilation factor (V.F.) approximates on a percentage basis the efficiency of the lungs as a bellows, and the value is determined from the average of three measurements, all expressed as per cent of the normal predicted, namely, the three-second vital capacity, the maximal breathing capacity and the residual air capacity as per cent of total lung capacity.

to 61 mm. Hg. (Table II.) These data demonstrate that in chronic pulmonary disease the direct determination of arterial blood pH is the only accurate measurement of the exact status of acidosis or alkalosis in an individual case. The Cambridge glass electrode pH meter is about the size of a portable electrocardiograph machine and permits quick measurements of pH. Arterial puncture of the brachial or femoral artery is usually an easy procedure with a B & D Cournand type needle. A small amount of heparin is used in the luer-lok syringe to keep the blood from coagulating before the transfer of the blood to the Cambridge glass electrode without contact with air using the 1 cc. Van Slyke blood pipette.

Although the arterial pCO_2 may be elevated in emphysema, the arterial pH is usually in the normal range in the absence of cardiac failure or respiratory depression of drugs, anesthetics, infections or other acute changes. The arterial pCO_2 is a function of alveolar aeration, and by direct measurement arterial pCO_2 correlates well with the ventilation factor.[2]

VENTILATION MEASUREMENTS

The expired air from the patient is studied with respect to the minute ventilation (total volume of air breathing during a test period of three to five minutes), the total oxygen uptake and the percent of oxygen extracted from the inspired air breathed. The minute ventilation is measured with respect to the number of L. per minute per square meter of body surface area. If the minute ventilation as L. per minute per square meter body surface area is below the normal range (2.6 to 3.8 at rest and 8 to 10.5 with step-up exercise for one minute), hypoventilation is indicated and, if above, hyperventilation. The minute volume of ventilation divided by the respiratory rate gives the average tidal volume, and the effective tidal volume that actually reaches the alveoli may be calculated from the expired pCO_2 and the arterial pCO_2. The data from two sets of resting measurements obtained at the same study period about two hours apart are given from a patient in Table III showing the effect of the minute ventilation and tidal volume on the blood gas exchange, one a rapid shallow type (Rest I) and the other more nearly normal (Rest II). Note that the dead space ventilation is about the same in both, but that the effective tidal ventilation is almost doubled in Rest II with marked differences noted in the blood gas exchange as shown in Table III. In some cases hyperventilation may be the only abnormality revealed from the pulmonary function evaluation. The one-minute step-up exercise test (thirty steps on an 8-inch stool in one minute) has been standardized with respect to the normal range.[1] In some cases of marked pulmonary insufficiency the exercise minute ventilation may be inadequate in proportion to the step-up test requirement. In general, the minute ventilation as a single measurement is often indeterminate as revealed from extensive statistical studies on a large series of cases. The minute ventilation along with the data provided from the expired air gas analysis provides the necessary data to calculate the oxygen uptake. The oxygen uptake is determined both at rest and with exercise. The resting oxygen uptake tends to be in the normal range regardless of the degree of pulmonary insufficiency,[11] hence, is of little value in pulmonary disability evaluation. On the other hand, the measurement of step-up exercise oxygen uptake is a very significant value. A marked reduction in the exercise oxygen uptake (normal range 500 to 600 ml. per min. per square meter body surface area) in the presence of an adequate minute ventilation reflects the inability of the individual to expand the pulmonary bed and

TABLE III
EFFECT OF VENTILATION VOLUMES ON BLOOD GAS EXCHANGE

Measurements	Rest I	Rest II
1. Respiratory rate, per min.	23.3	17.3
2. Minute ventilation, L./min.	5.26	8.34
3. Tidal volume, ml.	226	482
4. Effective tidal volume,* %	55.0	65.0
5. Effective tidal volume, ml.	124	315
6. Effective tidal ventilation, L./min.	2.89	5.45
7. Dead space ventilation, L./min.	2.37	2.89
8. Oxygen content, vol. %	16.88	19.40
9. Arterial blood oxygen saturation, %	83.4	95.5
10. CO_2 content, vol. %	45.33	41.05
11. pH	7.46	7.54
12. pCO_2, mm. Hg	40.8	30.7
13. pO_2, mm. Hg	63.1	106.6

* Calculated from the expired pCO_2 and arterial pCO_2.

increase the pulmonary blood flow or to increase the cardiac output from the right heart to the elevated level representing a normal response proportionate to the degree of exercise given.[1,11] If the normal amount of oxygen is removed from the expired air during the one-minute step-up exercise, an increased blood flow is necessary. If the oxygen uptake is normal during exercise, this indicates that the pulmonary blood flow is increased in proportion to the degree of exercise and that the pulmonary vascular resistance is not significantly altered. A decreased oxygen uptake during step-up exercise in the presence of an adequate minute ventilation indirectly indicates increased pulmonary vascular resistance, without the necessity of catheterizing the right heart to measure mean pulmonary arterial pressure and the cardiac output.

The per cent of oxygen extracted from the inspired air breathed is a measure of the lung ventilation efficiency, and this figure is used to determine the oxygen uptake along with the pulmonary ventilation volume measurement. Normally 4 to 5 per cent of the oxygen is extracted from the inspired air at rest and 5 to 6 per cent during the step-up exercise. Thus if a patient is removing only 2.5 per cent of the oxygen from the inspired air during exercise, twice the normal volume of air would be required for breathing to furnish the oxygen. In chronic pulmonary disease the per cent of oxygen extracted from the inspired air is usually decreased somewhat, but this measurement is usually indeterminate as to the degree of pulmonary function impairment present unless the decrease is of a very marked extent. Excitement with hyperventilation may result in a very low abnormal value, which might be normal if the individual were breathing at a lower volume rate. A patient with a severe degree of pulmonary insufficiency may have hypoventilation present during the step-up exercise and show a normal per cent of oxygen extracted, but the total oxygen uptake would be decreased markedly.

PRESSURE BREATHING

Intermittent positive pressure breathing (IPPB) consists of an active inflation of the lungs during inspiration with a regulated positive pressure from the cycling valve providing a maximal peak pressure at the mouth adjustable usually from 10 to 20 cm. of water. After the valve cycles expiration occurs as a passive deflation produced primarily by the elasticity of the lungs and the chest wall structures. The cycling of the respirator valve follows the patient's pattern of breathing. Factors to be considered in using IPPB are related to the shape and duration of mask pressure applied at the mouth, namely, the time relation of inspiration and expiration, the cycling rate and the magnitude of pressure applied (maximal, minimal and mean).[15,16] The most desirable type of mask pressure curve to apply to the mask or intratracheal tube is a gradually increasing pressure during inspiration and rapidly dropping to atmospheric early in expiration, expiratory time equal to inspiratory time, and most of the mean mask pressure is exerted during the inspiratory period. This type of intermittent positive pressure breathing provides a high peak mask pressure effective in overcoming breathing resistance, yet the mean mask pressure for the entire respiratory cycle is low, so that normally no deleterious effects are produced on the pulmonary circulation. The use of intermittent positive pressure breathing for prolonged periods does not produce distention of the lungs or increase the amount of residual air even in patients with far advanced degree of pulmonary emphysema.[17] The instantaneous flow rate of respiratory appliances should be high, above 100 L. per minute, so as to meet the flow needs of the acute asthmatic or cardiac patients, otherwise increased negative intrathoracic pressure may develop during inspiration with subjective dyspnea.

In the postoperative phase the arterial blood oxygen saturation may be quite satisfactory from oxygen given by a catheter, mask or tent, but the accompanying decreased ventilation results in an inadequate elimination of CO_2 and respiratory acidosis develops unless mechanical respiratory assistance is provided by intermittent positive pressure breathing (IPPB). The IPPB increases pulmonary ventilation and may be safely given using the Halliburton, Bennett or the Emerson breathing units* with maximal peak pressure settings of 10 to 20 cm. of water. IPPB five to ten minutes out of every hour or half hour may be adequate during the critical period or as otherwise indi-

* Halliburton IPPB unit made by Duncan Oxygen Therapy Co., Duncan, Okla. Bennett IPPB unit made by V. Ray Bennett, Los Angeles, Calif. Emerson IPPB unit made by J. H. Emerson Co., Cambridge, Mass.

cated to keep respiratory acidosis from developing. The effectiveness of IPPB has been demonstrated for increasing alveolar aeration in cases with severe degree of pulmonary insufficiency with obstructive elements. The use of 60 per cent helium and 40 per cent oxygen with IPPB and bronchodilators is helpful in some cases to facilitate aeration around and beyond secretions and to carry bronchodilators to the area of spasm in the bronchioles and to provide a high inspiratory pO_2. In order for the patient effectively to cough up secretions, gas must be delivered beyond the location of the secretion. The great diffusibility of helium facilitates the carrying of the gas and bronchodilator substance to the site of the spasm and plugging in the bronchioles so as to treat the bronchospasm effectively and to move the air beyond the secretion in the bronchioles thus enabling the patient to expectorate more effectively. The use of helium with oxygen (not less than 30 per cent oxygen) has been found most helpful in cases of severe emphysema during acute episodes of pulmonary infection with marked plugging of the bronchioles aggravated by bronchospasm (status asthmaticus may be markedly benefited by the IPPB treatments).[6]

PULMONARY VASCULAR RESISTANCE

In normal individuals during exercise the cardiac output from the right heart may increase three times or more above the resting level without an increase in the pulmonary artery pressure because the pulmonary vascular resistance is decreased.[18] A gas breathing mixture containing low concentrations of oxygen (such as 10 per cent oxygen in nitrogen) produces a rapid lowering of the partial pressure of oxygen and per cent saturation in the arterial blood in man (acute hypoxia), elevates the pulmonary artery pressure (constricts pulmonary arterioles) and increases pulmonary vascular resistance.[19] In patients with chronic pulmonary disease the pulmonary artery pressure is usually elevated during mild exercise, although the cardiac output may be increased only 2 or 3 L. per minute, which in some cases represents the maximal response above the resting level of which the individual is capable. The inability to increase the pulmonary blood flow during exercise in a normal manner constitutes one of the major factors producing disability in chronic pulmonary disease. When the pulmonary blood flow is inadequate during exercise, the oxygen uptake from the lung is reduced, less oxygen is available for the body tissues and an oxygen debt develops. An adequate pulmonary blood flow is necessary to maintain normal gas exchange in the lungs both during rest and exercise. The blood must also contain sufficient hemoglobin to carry an adequate quantity of oxygen to the tissues.

SUMMARY

The physiology of respiration with reference to pulmonary disease has been discussed as related to the maintenance of a normal oxygen tension in the blood supplying the tissues and the adequate removal of carbon dioxide both during rest and exercise. Frequently patients with chronic pulmonary disease receiving oxygen therapy have normal saturations in the arterial blood, but this does not insure that carbon dioxide is blown off properly unless the alveolar aeration is maintained at an adequate level.

The important clinical aspects of respiration discussed are concerned with the maintenance of a normal respiratory state and include lung volume measurements, oxygen transport across the lung, carbon dioxide regulation, acid-base balance, ventilation measurements, intermittent positive pressure breathing and pulmonary vascular resistance.

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Pathogenetic Concepts of Some Aspects of Pulmonary Disease

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THE use of antibiotics in the prevention and treatment of suppurative inflammation of the lung, the advent of specific chemotherapy in tuberculosis, the use of streptokinase and streptodornase in pleural collections and the development of such procedures as bronchospirometry and pulmonary arterial catheterization in the study of pulmonary function have necessitated a re-evaluation of our concept of the pathogenesis and the complications of many forms of pulmonary disease. The pathology of this disease has to some extent been outmoded. It is doubtful whether any recent graduate from medical school can or will ever understand the real nature of pneumococcus pneumonia and its complications unaltered by modern therapy. Careful study of the numerous resected portions of lungs has enabled the pathologist and bacteriologist to study earlier phases of disease processes. The pathologist has also focused his attention on lungs from apparently healthy young individuals who have died suddenly from violence. More exact concepts of pathogenesis have emerged from these studies of early and incipient lesions. It is within this framework that some of the aspects of pulmonary disease as related to the practice of surgery will be discussed. It is difficult in a brief report to review the entire field. Attention therefore will be directed to such entities as post-traumatic and postoperative pulmonary changes, obstructive pneumonitis, lung abscess, bronchiectasis, fibrosis of the lung and pleura, emphysema and some aspects of pulmonary tuberculosis.

SOME ASPECTS OF TUBERCULOSIS

In the classic concept of tuberculosis there was a clear difference concerning the degree and significance of lymph node involvement as it occurred in the childhood type of tuberculosis (primary infection) and the adult form (exogenous reinfection or endogenous exacerbation). In the former, lymph node involvement was usually preeminent. The lymph nodes were large and associated with considerable caseation necrosis. Endobronchial tuberculosis as a consequence of this was not uncommon. In adults lymph node involvement was relatively insignificant and consequently endobronchial tuberculosis secondary to it was rare. The development of endobronchial tuberculosis as a complication of lymph node tuberculosis appears to be occurring proportionately to a greater degree in adults in recent years. In two current reports[1,2] perforation of caseous hilar lymph nodes into the bronchi of adults has been stressed. In one of the reports thirty-eight recent bronchial perforations and eighty-one residual perforations were found in 1,228 bronchoscoped adults with pulmonary tuberculosis. However, it is doubtful whether lymph node penetration into the bronchi is as important a factor in the pathogenesis of adult pulmonary parenchymal tuberculosis as some have stated.[3] In this country at least, the majority develop pulmonary parenchymal tuberculosis either from endogenous exacerbation of pre-existing parenchymal disease or from a new or primary infection caused by tubercle bacilli inhaled directly into the parenchyma from without. Because of the public health measures which have delayed, and frequently prevented exposure of individuals to significant doses of tubercle bacilli until young adulthood or later many of the current cases of adult tuberculosis are the result of recent primary infections. This probably accounts for the reported increase in the number of cases of adult tuberculosis with caseous lymph nodes that involve the bronchi. One may conjecture that chemotherapy combined with surgical resection may be permitting us to see this complication relatively more

frequently. Bronchial involvement secondary to hilar and peribronchial lymph node tuberculosis presents such variations as endobronchial tuberculous with exuberant granulation tissue, bronchial fistulas, focal scars, partial and complete stenosis, diverticulas and broncholiths. When endobronchial tuberculosis heals with scar formation, the wall becomes rigid and the lumen narrowed. The partial obstruction hinders the normal cleansing mechanism of the involved pulmonary segment and predisposes to suppurative inflammation and bronchiectasis. It is possible that a relatively greater incidence of bronchiectasis on this basis may be seen as a consequence of untreated adult endobronchial tuberculosis. The more obvious complication is the direct dissemination of tubercle bacilli into the area of lung supplied by the involved bronchus with the onset of segmental tuberculous pneumonia. Occasionally obstructive emphysema is a prominent complication.

Perhaps no other problem in recent years relative to the therapy of tuberculosis has raised as much of a controversy as the method of treating the isolated subapical necrotic focus which persists after intensive and prolonged chemotherapy. This lesion often persists without any clinical manifestations of the disease. A number of years ago studies[4] on these isolated necrotic foci clearly demonstrated that significant numbers of these lesions communicated intermittently or persistently with the bronchial tree. This was in contrast to what had been previously reported by others. However, there is no doubt that at present that these foci communicate with one or more bronchi. A necrotic focus may represent an original area of caseous pneumonia which has not completely liquefied; it may represent an incompletely healed cavity with inspissation of the caseous material or it may represent a "tuberculoma." These lesions are potentially dangerous because it is unusual for them to resorb and difficult for them to organize or to slough completely so that viable tubercle bacilli can persist in them for long periods and eventually be disseminated. Because these areas are hardly ever irrevocably sealed off from the bronchial tree, reopening may occur despite any form of nonsurgical therapy. The ultimate disposal of these necrotic areas presents a major problem. Closely related is the unsolved question pertaining to those factors responsible for the liquefaction of the necrotic caseous material. It is well known that in some cases this necrotic material will liquefy almost immediately while in others solid isolated necrotic foci may persist for years, and then for reasons not completely understood, suddenly liquefy with the discharge of tubercle bacilli into the communicating bronchi. Some[4] claim that liquefaction results from the action of proteolytic enzymes released from lysed polymorphonuclear leukocytes that infiltrate the area. Others[5] believe that the enzymes responsible for liquefaction of the lesions are derived from the tubercle bacilli or the products of the inflammation.

Many of these lesions which did not show any alteration following adequate and prolonged chemotherapy were then resected. Study of them provided further proof of the concept that these were potentially harmful lesions since they communicated with bronchi. Furthermore cavities and foci of necrosis were found that were previously unsuspected from the x-ray picture and clinical examinations. It was also demonstrated that streptomycin promoted healing with an increase in the extent of epithelialization at the bronchocavitary junction.[6] Although this is a manifestation of healing, it has its adverse effects. An epithelial lining at the bronchocavitary junction could prevent complete closure by interfering with the approximation of the opposing granulation tissue surfaces. This, at least theoretically, increases the danger of those isolated solid, necrotic, or partially cavitary foci.

The problem became even more complicated when bacteriologic studies performed on these resected isolated lesions (previously treated with chemotherapy) revealed that the acid fast bacilli could be stained on smears (obtained from these necrotic foci) but too often failed to grow on artificial culture media and in many instances were no longer pathogenic for the suitable experimental animal.[7] Thus the "burning" question of the day concerns the viability of these organisms. If dead, perhaps resection is not as frequently justified. At this stage of inconclusive and conflicting evidence it would seem prudent to regard these bacteria if not actively alive, as at least sound asleep, rather than dead. This is consistent with the demonstrated biologic behavior of other single cells. Some pathogenic bacteria as well as cancer cells from experimental tumors

FIG. 1. Section showing acute necrotizing inflammation of bronchiolar wall. Hematoxylin and eosin, × 100.

may be lyophilized, frozen and kept in this apparently dormant state for long periods of time (years) only to be rejuvenated and then under proper conditions to produce infection or malignant growths. Although the most recent studies are in favor of viability, the final answer must await more careful bacteriologic, biologic, genetic and biochemical investigations. Upon this determination will depend the most rational form of treatment of the persistent caseous focus.

At the operating table the surgeon frequently notes more disease in the lungs than was anticipated from the x-ray picture. The question arises of how much lung to resect. Should the subapical necrotic focus alone be resected or is it necessary to remove the entire lobe because some nodules are present in the lower portions of the lobe? An important determining factor in the behavior of a tuberculous lesion is its location in the lung. All other factors being equal, the higher the lesion is located in the lobe the less is the chance for healing. Posture is of considerable importance in pulmonary tuberculosis.[4] For instance in cattle, tuberculosis flourishes best at the posterior basal regions of the lungs. This area, however, is actually the highest portion in a four-legged animal. Untreated hematogenous miliary tuberculosis in adults as it progressed will eventually reveal more numerous, more necrotic and larger lesions in the higher portions of the lung whereas in infants who are not uppright animals, this does not take place. It is believed that the difference in intravascular oxygen tension at various levels in the lung may be an important reason for this postural differentiation. At any rate, it may be necessary to resect only the necrotic focus in the upper portion of the lobe and then reasonably expect the lower lesions to heal with proper medical therapy.

With the prolongation of life as a result of chemotherapy, tubercle bacilli over a period of many years may at varying intervals spill from these recalcitrant necrotic foci. The bronchial and peribronchial lesions that result may remain subclinical. These multiple lesions may heal with the subsequent development of peribronchiolar fibrosis and bronchiolar narrowing with the production of obstructive emphysema. In some cases the process may be sufficiently extensive so that significant cardiorespiratory insufficiency is present.

COMPLICATIONS OF SUPPRATIVE INFLAMMATION (ABSCESS AND BRONCHIECTASIS)

Two of the main consequences of suppurative inflammation of the lungs are bronchiectasis and lung abscess. Many theories have been advanced for the pathogenesis of bronchiectasis. Among these are the ones concerned with congenital or developmental defects, distention of the bronchi by cough, destruction of the bronchial wall by necrotizing inflammation, obstructive mechanisms, atelectasis and fibrous retraction. The validity of all or some of these theories is still a matter of dispute, but one undeniable fact remains, and that is the importance of suppurative pneumonia in the development of bronchiectasis. That so many cases of bronchiectasis have followed the suppurative streptococcic and staphylococcic pneumonias which may complicate pertussis, measles, etc., is of major importance. That bronchiectasis so seldom appears after pneumococcic pneumonia is also of significance. In pneumococcic pneumonia, although atelectasis may be present as well as temporary obstruction with exudate of the

smaller ramifications of the bronchial tree, there is usually no necrotizing inflammation of the lungs. The bronchial tree is only mildly inflamed and remains intact. This is in contrast to the pneumonias associated with childhood diseases. In these pneumonias the bronchial walls are often involved in an acute necrotizing process. The development of bronchiectasis is to a great extent dependent upon the destruction of the bronchial musculo-elastic layer. (Fig. 1.) Whether or not this destruction begins as an ulceration through the mucosa or as a diffuse necrotizing inflammatory process of the wall is immaterial. Once the musculo-elastic layer is destroyed it is replaced permanently by fibrous tissue. It has been demonstrated that this process takes place rapidly within a matter of weeks from its inception. The decrease in recent years in the incidence of new cases of bronchiectasis is most likely attributable to early and effective chemotherapy of these suppurative pneumonias. This has limited the degree of bronchial necrosis and further attests to the importance of suppurative necrotizing pneumonia as a leading factor in the development of bronchiectasis. There is indeed no room in this report for full discussion of the pros and cons of the various theories regarding the pathogenesis of bronchiectasis. However, any infection of the lung which terminates in suppurative necrotizing pneumonia is basic to the pathogenesis regardless of what other associated mechanisms may be present, whether these be obstruction, traction, atelectasis or retraction. Once bronchiectasis has developed and it does so rapidly (it is not a creeping process that develops over a period of years), a sequence of events takes place determined by the degree, type and location of the bronchiectasis. The dilated and altered bronchi which are often lined with squamous and non-ciliated epithelium favor the retention of secretions within the lung. Since the retained secretions are an excellent culture media, repeated infections occur with varying degrees of pneumonia which undergo organization. The untrammeled course of bronchiectasis with repeated episodes of pneumonia eventuates in a contracted functionless lung or segment of lung. This consists of fibrous tissue, varying degrees and stages of organizing pneumonia, dilated distorted and scarred bronchi partially lined with polypoid granulation tissue and an altered epithelium. Focal and diffuse areas of atelectasis and emphysema may be present.

In a review of 200 consecutive postmortem examinations on patients with bronchiectasis (prior to the advent of antibiotics and in whom resection was not performed), it was found that the cylindrical form of bronchiectasis offered a more favorable prognosis than the saccular form.[8] This is understandable because it is easier for exudate to stagnate in the saccular type. Another factor of importance was the location of the bronchiectasis. All other conditions being constant, bronchiectasis that was limited to the upper portion of the upper lobe ran a less hectic course than bronchiectasis in other regions. Cylindrical bronchiectasis that was limited to the upper portions of the upper lobes did not produce any significant clinical pathologic picture because of the ability to drain well. The main clinical import of bronchiectasis in this location was that of its confusion clinically with tuberculosis. Only if bronchiectasis was bilateral and widely distributed did sufficient obstructive emphysema arise to be clinically significant. Associated with this was pulmonary hypertension and cor pulmonale. On occasion, in the diffuse form the dilatations were located principally in the smaller bronchi (bronchiolectasis) and was mistaken for atypical forms of fibrosis of the lung, bronchial asthma with infection, etc. In these 200 cases the average age was 58.5 years of whom 44 per cent died directly from bronchiectasis or its complications. In 75 per cent there was multiple lobe involvement. Diffuse bronchiolectasis was present in thirty-eight cases. Lower lobes were the site of bronchiectasis twice as often as upper lobes. Cylindrical and saccular forms occurred with equal frequency and were often present together in the same case.

Is bronchiectasis reversible? Perhaps the question can be resolved if one separates bronchiectasis into functional and anatomic types. Functional or relative bronchiectasis may result from the collapse or compression of the lung with the consequent crowding and foreshortening of the bronchi. This is a relative dilatation with no anatomic alteration in the bronchial wall. If the lung parenchyma reverts to normal, the bronchi then follow along, and this functional, relative or pseudobronchiectasis will then disappear. However, if there is necrosis in the bronchial wall, particularly in the muscu-

lar and elastic layers with dilatation of the bronchi (an anatomic alteration), the process soon becomes irreversible.[9,10]

The complications of untreated or ineffectively treated bronchiectasis are recurrent pneumonitis with organization, spread of infection to other parts of the lung, abscess formation, pulmonary hemorrhage, brain abscess empyema and, rarely, amyloidosis. The development of prominent bronchopulmonary arterial shunts in bronchiectasis offers a possible explanation for some of the altered circulatory dynamics that arise in this condition.[11] It is a factor that must be considered in the evaluation of the findings in pulmonary function and arterial catheterization studies.

The other main complication of suppurative pulmonary disease is lung abscess. Lung abscess may develop from the aspiration of infected or foreign material, from obstruction of the bronchial tree, from liquefaction necrosis of a primary suppurative pneumonia (Friedländer's bacillus, pneumococcus type V, staphylococcus, etc.), from infected emboli, rarely from secondary infection in a pulmonary infarct, from secondary infection of congenital cysts and emphysematous bullae,[12] from a penetrating injury of the chest wall or from intra-abdominal infection that penetrates the diaphragm. The pathogenic organisms involved are usually multiple, are frequently anaerobic and are occasionally associated with various fusospirochetes. Of all these mechanisms the onset of lung abscess secondary to aspiration is the most frequent.

Any individual ordinarily has certain defense mechanisms which permit him to keep out or rid his upper and lower respiratory tracts of noxious material. These include an active reflex system (sneezing, coughing, gagging), etc. To function effectively these depend on an intact central nervous system and muscular apparatus (chest walls, diaphragm). In addition to this the ciliated and mucin producing epithelial lining of the upper and lower respiratory tract is an effective means for the trapping and the constantly sweeping out of foreign material from the respiratory tract. Consciousness therefore is an important factor in maintaining the integrity of this reflex system. During such periods as surgical anesthesia, postoperative states, alcoholic stupor, traumatic shock, cerebral injuries with coma, many elements of the respiratory tract defense and cleansing system are impaired. Particularly if poor oral hygiene is present, the aspiration of food particles and saliva laden with bacteria and saprophytes, will then lead to suppurative pneumonia, and one of its complications, pulmonary abscess. In many instances, one may rub a tongue depresser against the wall of the pharynx of an individual with a lung abscess and find there is a completely absent or markedly depressed gag reflex. It has also been observed that during periods of sleep it is possible to drop lipiodal into the open mouths of the sleepers and, on x-ray examination the following morning, find lipiodal present in the parenchyma of the lungs. This indicates that inadequacies exist in these protective mechanisms under certain conditions.

The aspiration type of lung abscess is characteristically located in the periphery of the lung and is segmental in distribution. Localization of these abscesses in the different pulmonary segments can usually be related to the posture of the individual. If the person is in a supine position and infectious material is aspirated, the most direct route would be into the superior segment of the lower lobe. When the patient is on his side, the most direct route for aspirated material would be into the bronchi of the posterior segment of the lower lobe or the axillary branches of the anterior segment. Occasionally, areas of involvement are seen which are not so readily explained.

Early in the course of a lung abscess there is an overlying fibrinous pleuritis. This partially seals off that portion of the pleura from the remainder of the pleural space. This, in addition to the peripheral and segmental distribution of the abscess, has been the anatomic basis for the one-stage surgical treatment of lung abscess. With the use of chemotherapy and antibiotics, many cases of suppurative pneumonia do not proceed to the stage of lung abscess. If an acute lung abscess is present, it may be aborted so that it does not become chronic and with adequate drainage, it may become completely obliterated. However, in many instances this is not the case. An abscess develops which at first is thin-walled, may or may not be loculated, and may communicate freely with more than one branch of the bronchial tree. The inner lining of this abscess consists of a pyogenic membrane and granulation tissue which may be friable and bleed moderately. As the abscess becomes chronic, the granulation tissue is trans-

formed into a dense fibrous wall, and the surrounding parenchyma consists of organizing pneumonia with some bronchiectasis. Large blood vessels may be present in the scar tissue and superficially located in relation to the cavity lumen. On occasion, serious hemorrhage may occur from ulceration of these vessels. The lining of the cavity may consist partially or entirely of granulation tissue, squamous epithelium or, in rare instances of a ciliated one-layered mucus-producing epithelium.

The dense, rigid, fibrous wall of the abscess impedes collapse with total obliteration. Complete healing is also prevented because the granulation tissue may be covered with squamous epithelium. Residual cavities, therefore, are frequent sequelae and act as potential reservoirs for the accumulation of secretions and thus provide an excellent soil for the growth of bacteria. This serves as a source for contamination of other parts of the lung and for the recurrence of acute inflammation in the cavity.

Residual lung abscess cavities occur much more frequently than is generally recognized. It constitutes an important late sequella of lung abscess which must be considered in the approach to the primary treatment of lung abscess.

The differentiation of an aspiration abscess from an infected cyst of the lung may at times be very difficult. Even in the presence of the entire previous history it may be impossible. Pulmonary cysts usually have poorly demonstrable anatomic communications with the bronchial tree in contrast to lung abscess. Pulmonary cysts are more often centrally located. A bronchiectatic abscess usually contains cartilagenous and muscular elements in its wall. Lung abscess associated with bronchogenic carcinoma is usually secondary to obstructive pneumonitis and less frequently caused by necrosis and infection within the tumor itself. The latter situation is often confusing clinically, especially when a small peripheral carcinoma with central necrosis and infection simulates a small cavity in the periphery of the lung. Such cases have been observed for long periods before carcinoma was seriously entertained as the diagnosis of choice. Usually in this type of case a segment of the wall of the cavity is irregular and thickened. This represents irregular necrotic tumor in the wall of the abscess. The complications of lung abscess are bronchopleural fistula, empyema, spreading pneumonia, pulmonary hemorrhage, amyloidosis and brain abscess. In most cases of brain abscess pleural adhesions are present and the route of spread is usually through the vertebral venous system.

ACUTE NON-AERATION OF THE LUNG

Probably no other diagnosis related to pulmonary disease has been abused as much as that of atelectasis. It is constantly being made when opacities are seen in roentgenograms of the chest in such situations as postanesthetic states, barbiturate narcosis, chest wall injuries, prolonged rest in the supine position, poliomyelitis, bronchial asthma, pulmonary infections with retention of thick, tenacious mucus or exudate, and aspiration of foreign material or foreign bodies. Yet, postmortem examination of the lungs in such conditions most often fails to reveal what is correctly defined as atelectasis. This discrepancy is probably due to a misinterpretation of the actual alterations that usually transpire in the lungs in the aforementioned conditions. Atelectasis, correctly defined, refers to the incomplete expansion of the pulmonary parenchyma at birth, or to the collapse of varying portions of previously aerated lungs during later periods of life. The usual mechanism which is thought to produce collapse of lung parenchyma is absorption of the alveolar air after the bronchus to a particular region has been obstructed. The other mechanism, compression of the lung, may be produced by alterations in the pleura, diaphragm or chest wall. In the former mechanism, bronchial drainage is impaired, while in the latter it is not, unless, associated intrapulmonary disease is present. In microscopic sections the walls of the alveoli, alveolar ducts and respiratory bronchioles are closely opposed to form slit-like spaces with the walls often paralleling each other. The alveolar capillaries appear to be dilated, but it has been shown that less blood flows through an atelectatic lung than a normal expanded one.

The findings[13] of congestion, edema and some reduction in the size of lung, with an infiltration of inflammatory cells in dogs with obstructed bronchi, would indicate that in many instances shadows appearing in the chest roentgenograms are at first primarily caused by congestion and edema. The reduction in the size of the lungs and the inflammatory exudate appear some-

what later. Within thirty-six hours it was necessary to consider the process as pneumonia.

Sudden massive collapse of a lung or any portion thereof cannot be adequately explained on the basis of resorption of gas behind a blocked bronchus. Many hours must elapse before resorption would be complete. Massive collapse in sudden postoperative atelectasis is more readily attributable to a ball-valve type of obstruction which permits egress of gas during expiration but no ingress during inspiration. In a short period of time all the gas will be emptied from the lung and collapse will be complete. If the obstruction persists, edema and inflammation will appear.

Experimental observations indicate that the development of the edema is due to anoxia. The alveolar capillaries depend for their oxygen supply upon the alveolar gas. If this is shut off or reduced, the alveolar capillaries are deprived of sufficient oxygen and the capillary endothelium becomes more permeable. This permits fluid and cells to accumulate in the alveolar spaces. Another explanation offered for the development of edema, following bronchial obstruction, is a mechanical one. It is claimed, with absorption of gas distal to the obstruction, that a negative pressure is exerted on the alveolar capillaries with the resultant sucking of fluid from the capillaries into the alveolar spaces. It would seem from most experimental and clinical evidence that the former explanation is the most important and valid one. In some experimental studies obstruction of the larger bronchi has produced real atelectasis without edema. However, in these studies the bronchi were obstructed through an open chest and after the lung was collapsed from the pneumothorax created by the procedure.

In all of these conditions one of the most important defense mechanisms necessary to maintain adequate aeration of the lungs, that is, collateral ventilation, is interfered with. Maintenance of adequate collateral ventilation is dependent upon a proper functioning neuromuscular apparatus as well as the patency of the smaller bronchioles. In both experimental studies and in clinical experience congestion and edema developed very early from multiple causation. Any subsequent reduction in the size of the lung (atelectasis) would then be superimposed on this pre-existing edema and congestion.

The sum total of the final picture, depending on the duration and circumstances involved, is a combination of congestion, edema fluid, inflammatory cell infiltration and varying degrees of reduction in size of the lungs due to the absorption of gas. Without antibiotic therapy this is the ideal background for the development of pneumonia. Simple collapse of the lungs, as in compression atelectasis following artificial pneumothorax in which none of the above factors are operating, and in particular in which the bronchial drainage is not impaired, does not predispose toward infection. It is important to note that despite the terminology employed, whether this be atelectasis, wet atelectasis, collapse of the lung, edema or atelectatic pneumonia, what the mechanism and pathogenesis of the lesion is and what the ultimate consequences might be. The use of the term, acute non-aeration of lung, is suggested to describe these x-ray picture shadows because it is non-specific and yet recognizes the fundamental functional and anatomic alteration that is present. In any individual situation of this sort it is difficult to be certain of the proportions of congestion, edema, pneumonia and actual collapse present on clinical and roentgenographic evidence. (Fig. 2.)

CHRONIC OBSTRUCTIVE PNEUMONITIS

Chronic obstruction of the bronchus leads to changes in the parenchyma. Unfortunately, the term "atelectasis" has been indiscriminately applied to these changes. The use of the term "atelectasis" persists despite reported observations that have carefully detailed the changes as not being those of atelectasis. The most important cause of chronic bronchial obstruction is carcinoma. Bronchogenic carcinoma in its early stages does not produce complete obstruction. At the stage at which there is incomplete obstruction, there is interference with the normal defense or cleansing mechanism of the lung. This impairment consists of mechanical obstruction, destruction of ciliated epithelium and muscular elastic layer of bronchus. As a result, infection flourishes in the particular segment of the lung involved. This infection may consist of such changes as suppurative pnuemonia, bronchiectasis and/or lung abscess with organization of this pneumonia. Recurrences of pneumonia with repeated organization eventually produces a contracted fibrotic and chronically inflamed segment or lobe of lung. This is the character-

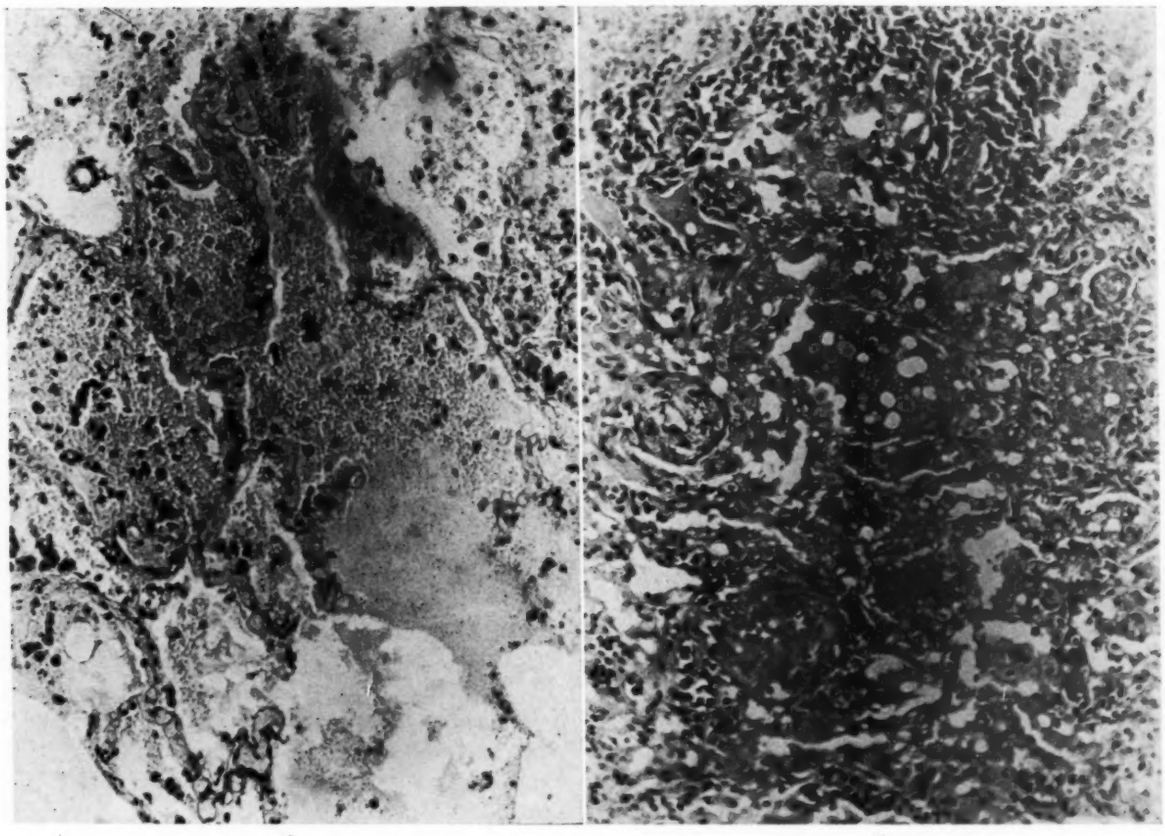

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FIG. 2. Section showing an area of acute non-seration following trauma to the chest. Intra-alveolar edema fluid, red blood cells and some mononuclear cells are present. Hematoxylin and eosin, × 250.

FIG. 3. Section showing pneumonitis secondary to chronic bronchial obstruction. Hematoxylin and eosin, × 230.

istic picture of chronic obstruction in the bronchial tree, and should be regarded as chronic pneumonitis rather than as atelectasis. By the time the bronchus is completely obstructed, these changes have all taken place and one is usually dealing with a functionless area of lung. The question of whether or not some air has been resorbed to produce superimposed atelectasis is quite irrelevant. Bronchial adenoma, foreign body, mucus inspissation and broncholiths, etc., will produce the same picture of obstructive pneumonitis. On occasion, there may be suddenly engrafted on this partial obstruction, hemorrhage, edema or necrosis of tissue, which then for a period of time completely obstructs the bronchus. Associated with this gradual organizing pneumonitis there may then develop acute non-aeration consisting of an admixture of edema and collapse. (Fig. 3.)

From a diagnostic and pathogenetic viewpoint it should be recognized that in this antibiotic era it is entirely possible for suppurative pneumonia to resolve almost completely despite the persistence of the bronchial obstruction. However, inevitably infection will recur in this same segment of the lung. Obstruction is only one cause of unresolved and organized pneumonia. When an area of pneumonia fails to resolve, it should be realized that there is an underlying reason for this. One of the most important reasons has already been mentioned, namely, obstruction of the bronchus. In other instances failure to resolve is based upon an underlying and often previously unrecognized bronchiectasis, primary suppurative pneumonias such as Friedländer's, unrecognized tuberculous pneumonia, lipoid pneumonia, etc. In recent years there has been discussion of an entity which has been called cholesterol pneumonitis. In the author's opinion this merely represents an excessive accumulation of lipids (cholesterol in macrophages) in an area of organized pneumonitis

from whatever the cause. Some in the past have referred to this as a "golden pneumonia." This is in no way different than lipid accumulation that is seen in chronic salpingitis or the high cholesterol content of the exudate in chronic empyema. Endogenous accumulation of lipids in chronic inflammation is not unusual and should not be regarded as a distinct entity in itself.

FIBROSIS OF THE LUNG AND PLEURA

Discrepancies are frequently noted between the degrees of lung involvement shown by the roentgenogram and the severity of the subjective symptoms of the patient. With the advent of pulmonary functional studies, such as bronchospirometry, pulmonary arterial catheterization, discrepancies were still observed between the degree of functional impairment and the degree of involvement on the x-ray picture. It is also well known that there is often very little correlation between cardiorespiratory insufficiency that is observed in silicotics and the degree of pulmonary involvement as seen both on the roentgenograph and at postmortem examination. An analysis of postmortem examinations on a great variety of pulmonary conditions, however, indicate that it is the pattern and the distribution of the fibrosis of the lungs rather than the quantitative degree of fibrosis that is more closely correlated with the severity of both the objective and subjective clinical manifestations.

These patterns of fibrosis will, to a great extent, determine the degree and type of ventilatory (air-flow), respiratory (gas exchange at alveolar interspace) and combined ventilatory and respiratory and cardiopulmonary disturbances. An understanding of the means, whereby the different patterns of fibrosis disturb pulmonary function, would to a great measure explain apparent discrepancies between the degree of both subjective and objective pulmonary disturbances in the patient and that which is seen on the roentgenographic picture. The status of pulmonary function at any given time depends on the dynamic interplay of the anatomic alterations caused by fibrosis, variations of blood supply in volume and composition, the condition of neuromuscular apparatus of the chest and the chemical stimulation of the brain centers.

In many disease entities several different patterns of fibrosis may coexist. The destructive effects of inflammatory and neoplastic processes on the pulmonary parenchyma are well known. Aside from these effects, probably the most significant results of damage to the lungs are secondary to the alterations associated with fibrosis. It is this fibrosis of the lung which results from various forms of injury and disease that very often determines the functional potential of the patient. Fibrosis of the lung may be distributed in five different patterns, namely, bronchial, interstitial, parenchymal, vascular and pleural. The types of fibrosis observed obviously depend upon the etiologic agent and the associated disease processes that produce fibrosis.

In the bronchial pattern of fibrosis, which may be secondary to any number of diseases, the most outstanding sequella is obstructive emphysema. This may be diffuse or local. Very often in diffuse obstructive emphysema there is minimal fibrosis in the alveolar walls. In contrast to the fibrotic alterations around the bronchial tree the alveolar walls reveal a delicate and alternated structure. The alveolar wall and blood vessel changes can be readily explained as secondary to the obstructive distention without the necessity of invoking primary degeneration of the lung parenchyma. (Fig. 4.)

The second pattern of pulmonary fibrosis is that which occurs in interstitial tissues of the alveolar walls. This produces primarily a disturbance of diffusion of gases across the alveolar capillary membranes. One of the classical conditions in which this type of fibrosis occurs has been called acute diffuse interstitial fibrosis of the lungs. However, the clinical and anatomic picture may also be subacute. In many other conditions the fibrosis is also predominantly in the interstitium of the lungs. Among these are scleroderma, beryllium poisoning and bauxite pneumoconiosis. This type of fibrosis not only causes a respiratory type of disturbance but it also increases the viscosity of the structural framework of the lung and thereby contributes to a ventilatory disturbance as well. (Fig. 5.)

Another pattern of pulmonary fibrosis is parenchymal or intra-alveolar. This is a common form and is often secondary to organization of any suppurative pneumonia, Friedländer's pneumonia, lipoid pneumonia and radiation pneumonia. The degree of functional impairment is almost quantitatively related to the size of the area involved and, to some

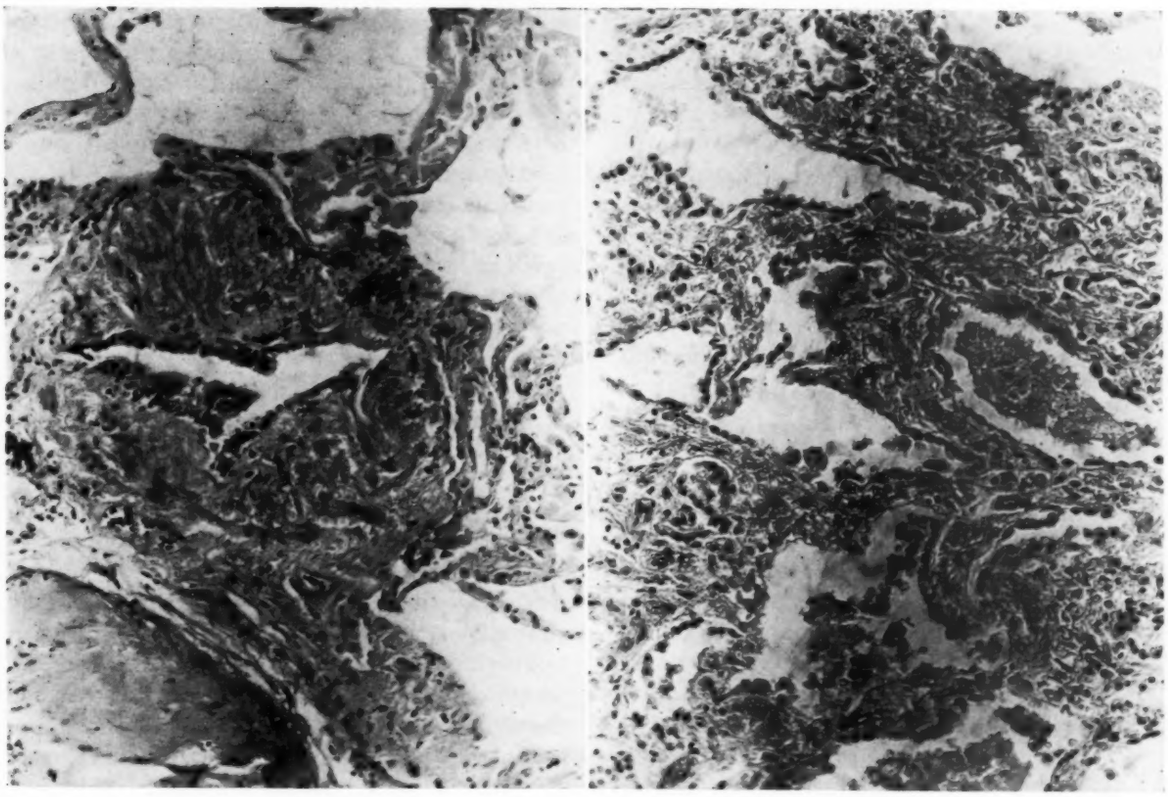

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FIG. 4. Section showing peribronchiolar pattern of fibrosis. Some muscle hyperplasia is also present. Hematoxylin and eosin, × 230.

FIG. 5. Section showing interstitial pattern of fibrosis with markedly thickened alveolar walls lined with prominent epithelium. Hematoxylin and eosin, × 250.

extent, to the degree of secondary compensatory distention emphysema.

Fibrosis or sclerosis of the pulmonary vascular bed is a fourth pattern, and is seen in such entities as organization of multiple arterial emboli or thrombi, pulmonary schistosomiasis, foreign body emboli in the pulmonary vasculature, etc. Organization of multiple pulmonary emboli has been mistaken for pulmonary arteriolarsclerosis associated with so-called primary pulmonary hypertension.

A well recognized form of fibrosis is that related to the pleura. This may result from organization of the exudate which develops secondary to acute or chronic pyogenic empyemas, tuberculous empyema or traumatic hemothorax. The fibrinous, serofibrinous, fibrinopurulent exudate or blood present in these conditions becomes organized, and a fibrotic pleural envelope develops, which contracts and constricts the underlying lung parenchyma. This eventually interferes with both the ventilatory capacity of the lungs and also with the flow of blood to the underlying involved area. A secondary effect is the development of distention emphysema in the uninvolved areas and/or in the contralateral lung. Sometimes in extensive and long-standing pleural involvement the fibrous tissue may extend along the interlobular septa into the lung parenchyma. This has the additional effect of diminishing the elasticity of the lung and hence further compromises ventilation.

With the development of the surgical procedure whereby these fibrotic pleural envelopes may be removed (decortication) and the lung re-expanded, it has become increasingly important to determine the amount of return to normal function that may occur after re-expansion of a long-standing compressed lung. Present studies seem to indicate that complete restoration of function does not occur despite complete anatomic re-expansion. This may be accounted for by the fact that in most cases, with fibrotic pleural envelopes there is associated underlying parenchymal disease. Best results would be obtained when the fibrotic pleural envelopes have appeared secondary to

traumatic hemothorax and when there was no associated pulmonary disease. The re-expansion of the lung will prevent the progression of distention emphysema in the contralateral lung. A distinct line of cleavage may be obtained in many instances between this pleural envelope which consists of organized exudate or blood and the underlying pleura. The peel (organized exudate) that is stripped from the visceral pleural surface often has adherent to it the outer layers of the pleura which contain elastic tissue. Failure to remove or prevent fibrothorax in children may result in extensive chest deformity.

EMPHYSEMA

Emphysema may be classified into three types: First, senile emphysema, in which there is supposedly an alteration in the composition and elasticity of the alveolar walls, with attenuation and degeneration of these walls leading to fusion of many of the alveolar spaces. There is no enlargement of the lung and no obstructive element is present in the bronchial tree. The lesion itself is without much clinical or functional significance. As a matter of fact, many no longer regard this form of emphysema as a distinct entity.

The second type is compensatory anatomic distention emphysema. This is seen after destruction, resection, compression or fibrous contracture of portions of the lung. The remaining lung tissue distends in order to fill in the abandoned space. It is, therefore, compensatory only in an anatomic sense, because any overdistention of the lung leads to functional impairment.

The most important form of emphysema is the third type and has been called by various observers, obstructive, idiopathic, large lung emphysema or degenerative lung disease. This may be diffuse or localized. Early stages of this form of emphysema are reversible, provided the obstruction has not been in existence to the extent that the integrity of the alveolar wall or its elasticity is permanently impaired.

In obstructive emphysema, large bullae (giant air cysts—pneumatoceles) may form. One of the mechanisms responsible for the development of these bullae is a chronic organizing constrictive bronchiolitis or peribronchiolitis which stiffens the walls and narrows the lumens of the bronchioles.[14] In those instances in which the muscular and elastic tissues are damaged and replaced, the mechanism, which normally regulates the tonus of the wall and the caliber of the tube, is impaired or destroyed. The total effect is an abnormal narrowing of the bronchioles. While inspiratory expansion of the contiguous parenchyma would partly open these to permit the passage of air, unusual inspiratory force would be required because of the constricting lesions. In the succeeding expiration the caliber of the bronchioles would be reduced below normal, partly because of the constricting lesions, and partly because of the loss of the masculoelastic tonus. This would delay the emptying of pulmonary lobules, which in consequence would be distended. As the chronic constrictive process increases during months or years, the functional effect would be aggravated, and as the distention of the alveolar tissue increases and the expiratory deflation becomes further retarded, the distended lobules, occupying increasing space, would tend during expiration to exert pressure against the walls of the enclosed bronchioles and possibly to stretch them. In this way a vicious circle is set up, until eventually the bronchiole, structurally and functionally, becomes quite insufficient especially during expiration, thus operating as a check valve. The chronically distended alveoli receive a diminishing blood and oxygen supply and would undergo the familiar changes of atrophy and disruption. The multiplicity of the constrictive bronchiolar lesions account in a large measure for the multiplicity of bullae. The presence of tenacious mucus in the bronchial passages might aggravate the mechanisms described. The origin of these chronic bronchiolar lesions is speculative, but many of these individuals give a history of chronic bronchial catarrh. At any rate, once these bullae develop, they extend to the point where they may rupture, with the formation of spontaneous pneumothorax; or else as they enlarge, they may compress and embarrass adjacent areas of lung parenchyma. At time of rupture the tension of a plueral fibrous adhesion may prevent the bronchopleural fistulas from closing and permit the pneumothorax to continue. If a large blood vessel is in an adhesion which may be torn in the sudden collapse of the lung, serious bleeding may take place.

Spontaneous pneumothorax associated with rupture of emphysematous bullae is usually not associated with infection in the plueral space, unless an underlying pneumonitis is present at the time of rupture. This is in con-

trast to spontaneous pneumothorax which in previous years was frequent in pulmonary tuberculosis. Spontaneous pneumothorax associated with tuberculosis is either secondary to the rupture of a bulla (emphysema secondary to the fibrosis of tuberculosis) or is the result of a perforation of a tuberculous cavity or necrotic parenchymal focus into a non-obliterated pleural space. The pleural space is almost always infected in spontaneous pneumothorax associated with tuberculosis.

Bullae are devoid of any epithelial lining, and the inner surface consists of compressed alveolar walls and perhaps some granulation tissue. There may be more than one opening of the bronchial tree, but these are not easily discernible. On occasion these bullae may become infected during the course of a pneumonia and simulate lung abscesses, bronchiectatic abscess cavities or infected developmental bronchogenic cysts. On occasion, following infection a bulla disappears entirely as a result of obliteration of all its bronchial communications, so that the absorption of gas without any access to new air causes it to obliterate. Occasionally, a bulla may rupture interstitially with the dissection of gas into the tissue spaces of the lung. This is called interstitial emphysema. Although many use the term "bulla" and "bleb" interchangeably, their original conception and pathogenesis are entirely different. The bulla, as has been described previously, is the result of dilatation, degeneration and destruction of alveolar walls with large air sacs present within the pulmonary parenchyma (intra-alveolar distention). A bleb, however, is produced by direct trauma to the lung or from the rupture of a bulla with dissection of the gas into the interstitial tissue planes. It may then appear within the layers of the pluera and protrude as a blister on the surface of the lung.

Recent studies indicate there is an increase in the amount of muscle in the small bronchioles and alveolar ducts in emphysema. The relationship of this to bronchospasm, an important factor in this disease, is considerable. There is also an increase in the bronchial-pulmonary venous-collateral circulation in emphysematous lungs. The significance of this regarding the further progression of the condition and its relationship to the impairment of cardio-respiratory function await further study.

Diffuse obstructive emphysema is of major concern to the surgeon because it is a vital factor in evaluating the pulmonary reserve of the patient. There are two problems involved; first, the amount of anatomic distention emphysema which will follow removal of considerable portions of the lung and, secondly, the amount of obstructive emphysema already present in the remaining lung. Advanced stages of diffuse obstructive emphysema lead to marked ventilatory impairment, pulmonary hypertension and cor pulmonale.

SUMMARY

Some aspects of the pathogenesis of the basic alterations in emphysema, atelectasis, obstructive pneumonitis, pulmonary fibrosis, lung abscess, bronchiectasis and tuberculosis have been presented. These alterations were selected for discussion because they represent the main patterns of pulmonary change secondary to a wide variety of etiologic agents.

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The Hematologic Role of the Lung in Man

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THE primary function of the lungs in man is the transfer of oxygen from the inspired air to the arterial blood, together with the excretion of carbon dioxide from the venous blood in the expired air. Among the many other physiologic functions of great importance is the hemopoietic role of the lung which has recently received renewed attention. This paper is primarily concerned with the participation of the lungs in the maintenance of a normal number of circulating formed blood elements including erythrocytes, leukocytes and platelets.

The crucial location of the pulmonary circulation, literally at the crossroads of the vascular system, appears to provide the lungs with the capacity of producing important changes in the volume of blood and its constituents by means of relatively small changes in pulmonary function. This appears to hold true for the gaseous content of plasma and hemoglobin, and for electrolyte equilibrium of the blood. The role of the lung in regulating the number of cellular constituents in blood appears to have received little attention until recently. Large, rapid fluctuations in the number of circulating formed elements which have been reported to occur indicate a prodigious yet facile reservoir which, under some circumstances, may cause an increase or decrease of 100 per cent within a few seconds. A review of both the old as well as the more recent findings is both feasible and meaningful in the light of newer technics of vascular catheterization with central and rapid sampling of blood, together with improved accuracy in the determination of the number of formed elements.

Erythrocytes. The erythrocyte serves primarily as a hemoglobin container whose integrity is essential for effective oxygen and carbon dioxide transport and for ion exchange. An intact cell membrane is necessary to retain the hemoglobin within the erythrocyte stroma so as to provide an oxygen-hemoglobin dissociation curve in a state favorable for the exchange of both oxygen and carbon dioxide.[1]

The lungs contribute in an important way, under other circumstances, to a more sustained stimulus for erythrocyte production. Prolonged states of hypoxia are followed by an increased regenerative activity of the bone marrow and subsequent compensatory increase in the number of circulating erythrocytes. This occurs both in persons with normal lungs residing at high altitudes, as well as for patients with lung disease or with congenital anomalies characterized by right-to-left shunts of blood and with chronic states of arterial oxygen desaturation. The consequence of this state of affairs is an increase in the total blood volume, attributable largely to an increase in red cell volume.[2] In this fashion the lungs may contribute to a sustained increased production of erythrocytes in the bone marrow. There is no change in erythrocyte number on the venous or arterial side of the lung. The exact mechanism by which lung disease and secondary hypoxia is followed by compensatory polycythemia remains to be elucidated.

A reduction in the concentration of effective hemoglobin and in the number of erythrocytes may occur through the intervention of the lungs. This may occur as a consequence of the influences of noxious fumes (lead, nitrite) or by the operation of a removal mechanism effected by the circulation within the lungs. The possible existence of the latter mechanism is being explored.

Leukocytes. The leukocyte count in the circulating blood may double or diminish to one-half or less within a few seconds.[3,4] While these variations have usually been ignored or attributed to possible counting errors, the magnitude of the changes are often far in excess of such errors. In some instances, both in the normal and the leukemic individual, the white cell count may vary 400 or 500 per cent from the original level within a few hours.

Leukocytes may accumulate in the capillaries of many organs under specific circumstances and, similarly, leukocytes may be released from these storage sites by the proper stimuli. Clark,[5] Sandison[6] and Lowit[7] believed that the leukopenias were due to disintegration of

leukocytes in the circulation. Arneth[8] concluded that the profound leukopenia observed following the injection of foreign proteins, bacteria and certain drugs were due to widespread destruction of cells which were replaced by young cells from the hematopoietic centers. Similar findings were reported by Aschenheim.[9]

The concept of leukopenia being caused by sequestration into various organs is well established.[10] The organs and mechanisms involved, however, have not yet been defined. Momouye[11] found the capillaries of the bone marrow, lungs and intestines to be those chiefly involved. Nye and Barrs[12] found the lungs, liver and, to a lesser extent, the spleen to be concerned in this process. Ewing,[13] similarly to Andrewes,[14] reported the trapping of leukocytes in the liver and lung following the intravenous administration of bacteria. Wells[15] believed the liver and spleen to be predominantly involved, while Doan[16] emphasized the role of the spleen in the leukopenic states. Silverman[17] believed that leukopenia was attributable to mechanical filtration of leukocytes induced by endothelial swelling of the capillary wall. Seyderhelm and Oestrich[18] injected leukocytes tagged with Congo red into rabbits. These cells were taken up by the liver when injected into the splenic artery or portal vein. If injected into an ear vein, they accumulated in the lungs. Garrey and Bryan[3] believed that the liver and lungs were the main sites of sequestration of leukocytes and that the role of the spleen was less significant.

It is apparent that any mechanism which functions to control the level of the circulating leukocytes must have the ability to act either rapidly or slowly, to perform continuously or intermittently and to remove or contribute formed elements directly into the circulation as the situation dictates. These criteria of sequestration sites can best be met by those organs which are exposed to large volumes of actively circulating blood. The heart, lungs and great vessels receive more of the circulating blood per unit time than other organs. The lungs, which had received relatively little attention from this viewpoint, appeared to be the most promising site to examine.

EVIDENCE FOR REMOVAL AND RELEASE OF LEUKOCYTES BY THE LUNG

Removal of Leukocytes after Blood Transfusion. It has been commonly observed that although whole blood transfusions from normal donors will raise the erythrocyte count, there is no coincident rise in leukocyte number.[19] Minot and Isaacs[20] transfused 450 cc. of whole blood from a patient with chronic lymphatic leukemia (95.6 per cent lymphocytes, 89,000 per cu. mm.) into a patient in an advanced stage of lymphosarcoma who had 992 lymphocytes/cu. mm. At the conclusion of the transfusion the lymphocyte blood count in the recipient was increased to 3,600. Thirty minutes later the lymphocyte number had returned to 1,759/cu. mm.; by calculation the lymphocyte count should have risen to 12,000/cu. mm. No satisfactory clue to account for the missing lymphocytes was offered.

The pulmonary circulation of non-leukemic man has been shown to be capable of removing billions of leukocytes infused from leukemic donors.[21] (Fig. 1.) Whole blood transfusions containing up to 140 billion leukocytes were given intravenously within two to ten minutes. When large numbers of leukemic leukocytes were injected into the femoral artery, they successfully traversed the capillary bed of the lower extremity without alteration, as shown by frequent samples of femoral vein blood during the transfusion, yet they were selectively removed by the pulmonary capillary bed as they reached the lung and failed to appear in the arterial blood in significant numbers. Weisberger and Heinle,[22] and Ambrus et al.[23] showed that the lungs of rabbits and rats also function similarly in withdrawing intravenously infused leukocytes. During the first hour after infusion of leukocytes tagged with P-32 the activity was found primarily in the lungs. Within three hours most of the radioactivity was found in the liver and spleen. It is difficult, however, to ascertain whether this radioactivity represented radiophosphorus in the intact leukocyte or P-32 which had been released from the white cell by diffusion or cell destruction.

Removal of Leukocytes in Cross Transfusion Studies. The pulmonary circulation is also capable of removing leukocytes from the peripheral circulation in man for as long as twenty-five to thirty-five hours during interarterial cross transfusion.[24] (Fig. 2.) The continuous removal of leukocytes without change in blood flow suggests that intravascular margination of leukocytes or mechanical filtration are not solely responsible. Calculations

showed the number of leukocytes removed during these periods was far in excess of the amount of cell mass the pulmonary circulation could accommodate over this period of time; there must be a mechanism and route whereby the cells could be withdrawn from the circulation and a pathway for the draining of these cells or débris from the lungs.[24] Some of these cells may be destroyed, others stored or excreted in the sputum and still others may make their way back into the circulation by way of the intrapulmonary lymphatics or blood vessels. It is not known which of these three methods are primarily involved or their relative importance in the total picture of leukocyte removal in the lungs.[25]

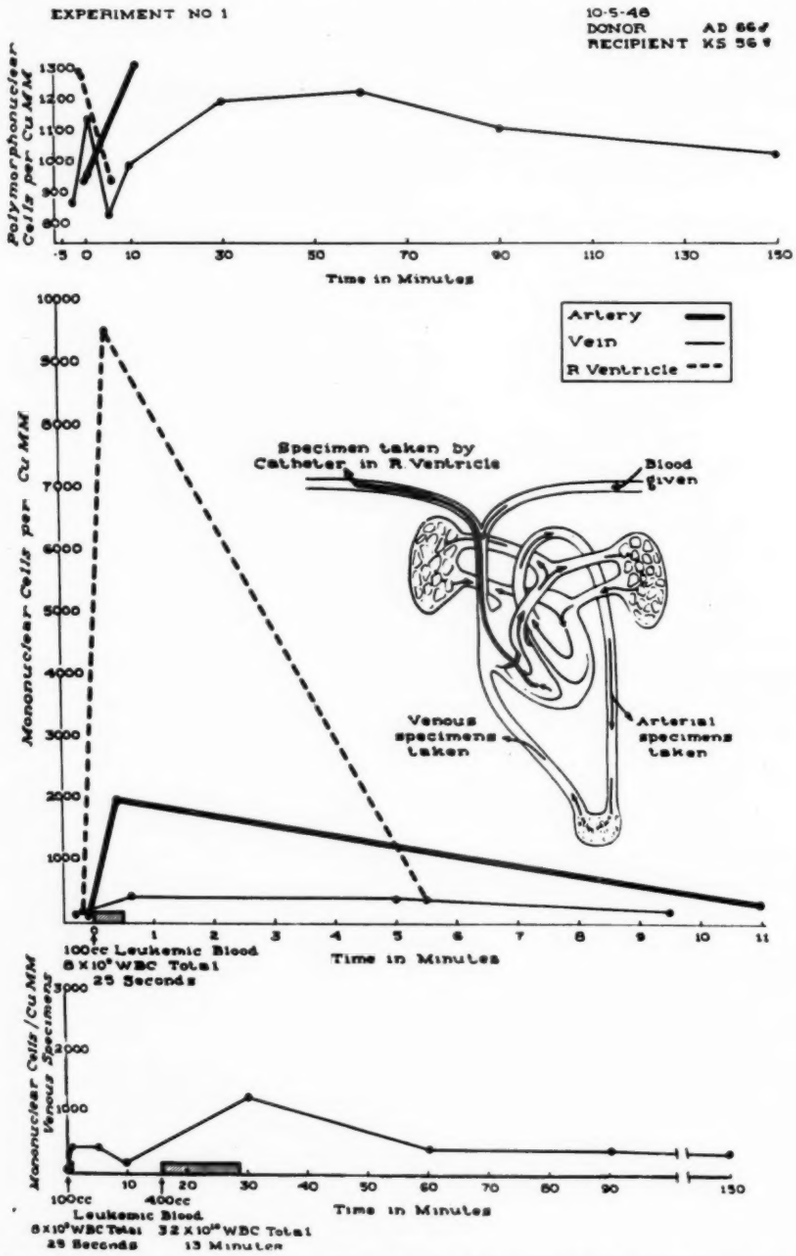


FIG. 1. Infusion of leukocytes from leukemic donor. Note marked discrepancy between samples taken from the venous and arterial sides of the lung. (From Lanman et al. *Blood*, 5: 1099, 1950.[21])

Changes in Leukocyte Levels during Respiratory Movements. Repeated observations of the leukocyte levels of blood sampled simultaneously from the right ventricle and left

ventricle or aorta frequently revealed significant differences.[26] At times the leukocyte counts in the venous blood exceeded that in the arterial blood, and a few moments later the arterial content of white cells was greater than that from the right ventricle. This freject in the pulmonary circulation during inspiration and expiration which is reflected peripherally by a constant variation in leukocyte level. The alterations that may occur in this mechanism under other physiologic and pathologic conditions remain to be elucidated.

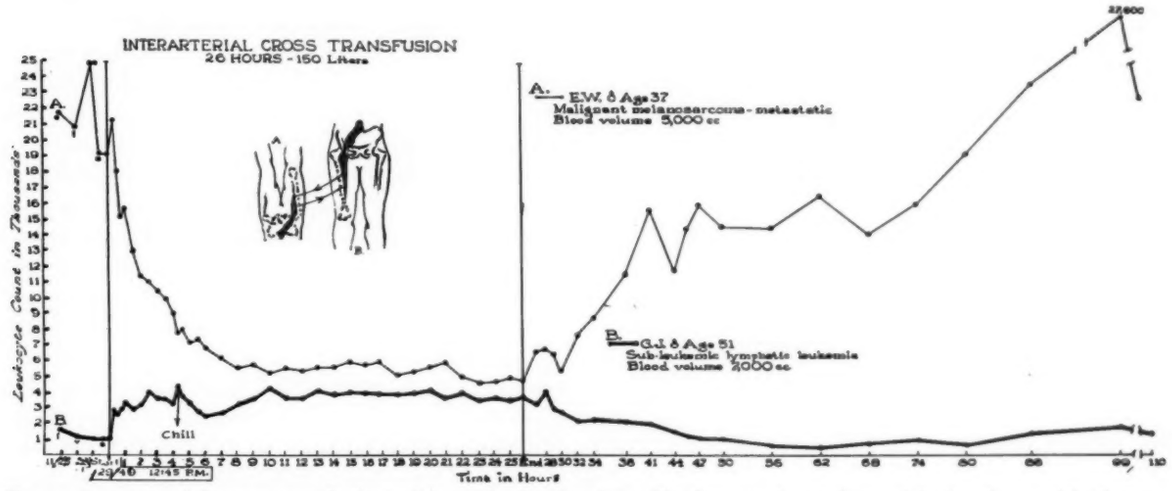


FIG. 2. Interarterial cross transfusion with marked reduction of leukocytes in patient with the elevated leukocyte level. All samples were arterial, and thus reflected blood coming from the lungs. (From Bierman et al., *Blood*, 6: 487, 1951.[24])

quent change in cell count on either side of the pulmonary circulation suggested some alteration of the number of leukocytes of blood passing through the lungs.

It was subsequently found that the arterial leukocyte count decreased significantly with a slight rise in the venous blood samples obtained from the right ventricle or pulmonary artery immediately after the initiation of the Valsalva maneuver. (Fig. 3.) This discrepancy persisted until toward the end of the forced expiration when the venous leukocyte level also fell. The leukocyte counts returned to their control levels after the Valsalva was released. During the Mueller maneuver, which is the physiologic counterpart of inspiration, both the venous and arterial leukocyte level exhibited an increase. Simultaneous leukocyte counts of both venous and arterial blood during prolonged inspiration and expiration similarly revealed a fall in leukocyte number in the arterial blood during normal inspiration and an increase with expiration. The granulocyte is involved almost exclusively. The magnitude of the fluctuations was greater and more consistent in the arterial than in the venous samples. These findings suggest that there is an ebb and flow of leukocytes in the normal sub-

The Influence of Pharmacologically Active Substances. Histamine: The rapid intravenous administration of histamine phosphate in doses of 0.1 to 0.3 mg. (as base) over a thirty to sixty second-period causes a prompt decrease initially in the peripheral arterial blood leukocyte number in the non-leukemic subject which is reflected twenty to ninety seconds later in blood from the right ventricle or peripheral vein, although not as profound as in the arterial blood.[27] This leukopenia persists for forty to 120 seconds, where upon the number of leukocytes in the arterial and venous blood increases simultaneously until the original level is regained. The leukopenia precedes the symptoms of dyspnea, flushing and headache so commonly associated with the intravenous administration of histamine. These findings demonstrate that the intravenous administration of histamine results in the transient sequestration of leukocytes within the pulmonary circulation until the peripheral arterial level of leukocytes falls. Subsequently, the circulating level of leukocytes returns toward normal.

The administration of histamine under identical conditions to most patients with lymphocytic leukemia fails to produce any

significant change in leukocyte number in either the arterial or venous blood.[28] Occasionally, however, transient leukopenia in the lymphocytic leukemic patient has been observed. Patients with monocytic leukemia respond in the same manner as non-leukemics

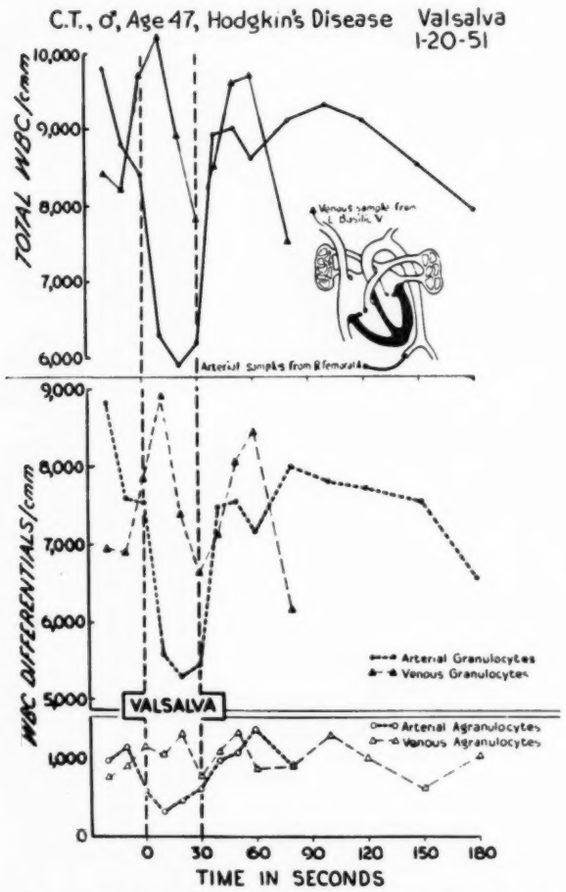


FIG. 3. Profound reduction in leukocyte number in the arterial blood simultaneous with a forced expiration. (From Bierman et al. *Blood*, 7: 533, 1952.[26])

and patients with granulocytic leukemia respond with a rise in leukocyte number. The data suggest that the pulmonary leukocyte removal mechanism in patients with lymphocytic leukemia and granulocytic leukemia does not respond to histamine in the normal manner.

In the past the fall in white cell count associated with intravenous histamine has been attributed to the pooling of the leukocytes in the capillaries of the spleen, liver and other splanchnic sites as a result of a fall in blood pressure. It is evident from these studies that the majority of cells do not pass the pulmonary circulation during the initial phase of intravenous histamine administration, and that the lungs are mainly responsible for the prompt leukopenia, albeit temporary.

Epinephrine: The leukocytosis following epinephrine will be discussed in detail in the section on platelets.

Saccharated iron oxide: The intravenous administration of saccharated iron oxide occasionally was found to be accompanied by granulocytopenia.[29] An investigation of the influence of this material upon the circulating leukocytes was undertaken.[30] The intravenous infusion of saccharated iron oxide in doses of 400 mg. or over and administered at a rate in excess of 100 mg. per minute resulted in arterial leukopenia which generally preceded that noted in the venous blood by at least one to two full circulation times. The leukopenia, attributable almost entirely to a fall in granulocytes, became progressively more profound and prolonged, the larger the doses employed and the longer the duration of infusion. When the venous blood was sampled proximal to where the iron was injected, all specimens collected during the period of administration and which consequently contained the largest amounts of iron promptly clotted within the collecting tubes despite an excess of heparin. All other specimens showed no such tendency. There was no significant alteration in the platelet counts.

In two patients with lymphocytic leukemia leukopenia was not obtained until repeated injections of iron had been administered for a total of 300 and 1,000 mg. It appears that saccharated iron oxide administered intravenously is capable of stimulating the withdrawal of leukocytes within the pulmonary circulation in non-leukemic individuals. Two patients with monocytic leukemia responded in the same manner as the non-leukemics, showing prompt leukopenia following the intravenous administration of colloidal iron.

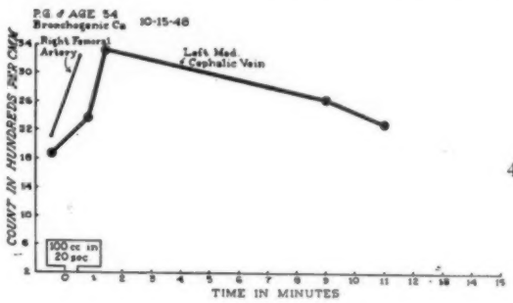
The Influence of Foreign Materials. Olitzki, Leibowitz and Berman[31] observed profound leukopenia following the injection of dysentery bacilli in two splenectomized animals. Olitzki[32] also found the polymorphonuclear leukocytes sequestered in the rabbit lungs during leukopenia resulting from typhoid vaccine. Some tolerance to the effect of pyrogens upon the leukocytes was suggested. However, this tolerance is apparently not related to the presence of circulating antibodies, behaved spasmodi-

cally and was reminiscent of the development of tolerance for fever.

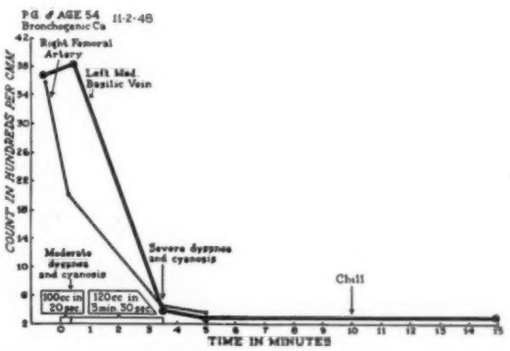
Dudgeon and Goadby[33] studied the tissue reactions in rabbits following intravenous injections of massive doses of India ink, colloidal silver, and both live and dead Staphylococcus aureus. They found that the particulate matter injected intravenously caused an accumulation of polymorphonuclear leukocytes in the lung capillaries. They also found an agglomeration of platelets about these particles. With live or dead Staph. aureus, some of the platelets were completely removed with the bacteria during phagocytosis with movement through the alveolar walls. There was phagocytosis of the inert particles by the endothelial cells of the lungs, liver and spleen, and the platelets were assumed to be restored to the circulation.

Changes in Leukocyte Level Produced in Anaphylactoid States. Pulmonary infarction, infections and metastatic lesions of the lung are often associated with leukocytoses of an extreme degree, yet occasionally patients with severe pulmonary infections will develop marked leukopenic states. Goldscheider and Jacob,[34] Bruce,[35] Andrewes[14] and Schilling[36] found that the lungs were filled with excessive amounts of leukocytes during leukopenia associated with anaphylaxis in rabbits and guinea pigs, and Webb[37] reported a similar finding in dogs. Andrewes[14] demonstrated that the pulmonary circulation of animals is capable of removing vast numbers of white cells with other immunologic stimuli. In a study of the accumulation of leukocytes in the lungs of rabbits following the administration of typhoid vaccine, Wells[15] concluded that the cells did not mass in the pulmonary capillary bed. However, his conclusions were based upon the counts of blood samples obtained by slashing the lung parenchyma with a razor blade. The microscopic sections of the lung capillaries contained excessive quantities of leukocytes but this data was apparently ignored in his conclusions. As Webb pointed out seven years later, blood obtained from "lung slashing" is mainly from the larger blood vessels, and the pulmonary capillaries, where the cells are sequestered, are not sampled adequately.

When pulmonary edema occurred during the course of a rapid transfusion of large numbers of leukemic white cells into humans, the pulmonary removal mechanism not only prevented passage of the infused cells but also removed great numbers of the white cells of the recipient. This was observed in two instances, in the first of which the initial study had been performed with the same recipient and donor two weeks previously. (Fig. 4 A and B.) During the first study there was no untoward reaction and the leukocyte count was essentially unchanged. The second transfusion was accompanied by marked and prompt leukopenia coincident with the sudden onset of dyspnea, tachycardia, pallor, basilar rales and other signs indicative of pulmonary edema.



4A



4B

FIG. 4A. The influence of infusion of leukemic leukocytes upon the eosinophil level in patient P. G. The other granulocytes acted in a similar fashion. The lymphocytes were too few in number to produce significant changes.

FIG. 4B. A repeat of study illustrated in Fig. 4A eighteen days later. Note marked eosinopenia occurring promptly after start of infusion associated with pulmonary edema.

The leukopenia observed in the second patient was also associated with the same symptoms during a similar but initial transfusion of blood from a patient with myelogenous leukemia.

In the first case a plausible explanation is one of sensitization of the recipient to the same donor's blood after a two-week period.[38] In the second patient the donor's blood had an inordinately large number of disrupted cells, the products of which may have been responsible.

Samter, Kofoed and Pieper[39] described the eosinotactic property of the lungs of guinea pigs following anaphylactic shock. This property of the lungs to produce eosinophilia upon intraperitoneal implantation into a normal recipient was not shared by the intestines, uterus, gallbladder, liver or skin. The lungs of normal or sensitized (but not reinjected) guinea pigs produced a significant but limited increase in the number of circulating eosinophils. This eosinotactic factor was largely inactivated by incubation at 58°C. for forty minutes.

It has been known that the lung is one of the major shock organs in both lesser animals and man. That it is also a site for the development of the eosinotactic factor presumably at the point of the antigen-antibody reaction is now being realized.

Chew and Lawrence[40,41] found that pyrogenic substances and the antileukocytic sera have identical effects and lung findings if they are administered intravenously, intraperitoneally or into the left ventricle. Both an antileukocytic and antilymphocytic serum also caused prompt leukopenia and neutropenia within five minutes following intracardiac injection. A one-week transient period of tolerance developed and acted similarly to the pyrogen tolerance.[42] Many of these findings were obtained in dogs, rabbits, guinea pigs and rodents.

The Effects of Tissue Extracts. Doan and his associates,[43] while studying the decrease in leukocyte count following the injection of crude nucleic acid extracts in rabbits, noted that the lungs as well as the spleen were sites of removal. Refined preparations of nucleic acids did not cause leukopenias as did the crude materials. This observation suggests that unrefined tissue extracts can stimulate the lungs to remove cells, since in some studies Doan observed leukopenia despite partial and total splenectomy.[43]

Weisberger and Heinle[22] have shown that material from destroyed leukocytes can cause prompt and profound leukopenia upon intravenous injection in rats and rabbits. The mechanism whereby such infusions of cellular debris initiates the removal of leukocytes by the pulmonary circulation involves the consideration of multiple pulmonary emboli by cellular particulate material as well as the cell constituents, both immunologic and chemical. Similar studies in man have shown this leukopenia to be initially and primarily arterial in nature.[44]

EVIDENCE FOR PRODUCTION OF PLATELETS IN THE LUNG

Howell and Donahue[45] showed that the arterial blood of dogs contains more platelets than blood from the right ventricle. This discrepancy existed in most, but not all observations, and was interpreted as evidence to indicate that the lungs of dogs produce and release platelets into the arterial blood. Megakaryocytes were shown to be present in large numbers within the dog lung and were presumed to be the source of the platelets.

Fidlar and Waters,[46] employing the heart-lung preparation of the dog, were unable to find supporting evidence for platelet production in the lungs. However, as they themselves pointed out, the heart-lung preparation may be unsuitable for such an investigation. Only one-fourth or less of the circulating blood volume of the dog was used for the perfusion and an initial rise in arterial platelet number was not sustained.

The administration of plasma obtained from a patient with idiopathic thrombocytopenic purpura into a volunteer free of any blood dyscrasia resulted in a prompt and profound fall in platelet level in the recipient's venous blood for two to four days.[47] When both arterial and right ventricular blood were sampled during such an infusion, the findings in the venous blood confirmed those of Harrington et al., but the platelet level of the arterial blood was maintained for approximately eight to eleven hours and then fell to coincide with that in the venous blood. (Fig. 5.) The lungs, therefore, must act either as a reservoir or as a site of production of platelets. The large numbers of platelets leaving the lungs for a prolonged period make it seem likely that new platelets were produced in the lungs under these circumstances. Whether the platelets are manufactured from megakarocytes in the lung in man, as Howell postulated in the dog, is questionable in view of the relative paucity of megakaryocytes in the human lung. It is more plausible that some other mechanism for platelet formation is involved.

The platelet count was found to rise promptly, exceeding the normal limits, immediately after the start of a cross transfusion.[24] (Fig. 6.) Similar findings were observed after

transfusions of granulocytic leukemic blood. It has again been suggested[25,48,49] that some white cells are trapped and broken up in the lungs with the release of leukocyte fragments which are recognized as platelets on the smear. These fragments appear to be morphologically identical with the classic description of platelets.

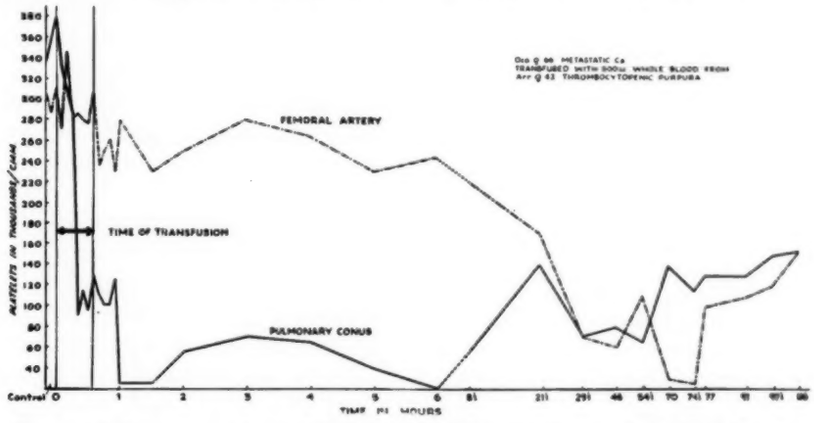


FIG. 5. Maintenance of arterial platelet number despite marked thrombocytopenia in the venous blood induced by the infusion of blood obtained from a patient with idiopathic thrombocytopenic purpura.

The lung contains a large amount of thromboplastin. Potent extracts which possess the ability to produce prompt clotting can be derived from lungs of both animals and man. Whether the lung manufactures platelets or thromboplastin, or just stores platelets or thromboplastin-like material has not been clarified.

Abnormal forms of platelets are frequently found in the blood in the leukemias and chronic thrombocytopenias and in other conditions in which there is great alteration in myeloid tissues.[50] The lungs of patients with granulocytic leukemia and Hodgkin's disease are often excessively filled with megakaryocytes.[51,52] Repeated auricular punctures in leukemic patients have shown a greater number of megakaryocytes in blood from the right auricle than from the peripheral circulation, an indication that some may be arrested in the pulmonary capillaries. Ara[53] and Polletini[54] found that the entire contents of the vessels of the lung in some conditions may be made up of platelets.

Effects of Epinephrine upon Release of Platelets and Leukocytes from the Lung. The administration of epinephrine is usually followed by leukocytosis and thrombocytosis which is commonly attributed to a splenic contraction,[19,55,56] but is more likely from a pulmonary source.[57] However, a similar increase in leukocytes and platelets has been observed in the same patients following splenectomy[58] and more recently the role of the spleen following epinephrine administration has been questioned.[59] Hemoconcentration,[60] expulsion of leukocytes from lymph nodes[61] and redistribution of the formed elements of the blood have been suggested to explain these findings, but no specific site or organ has been designated as an additional source of platelets.

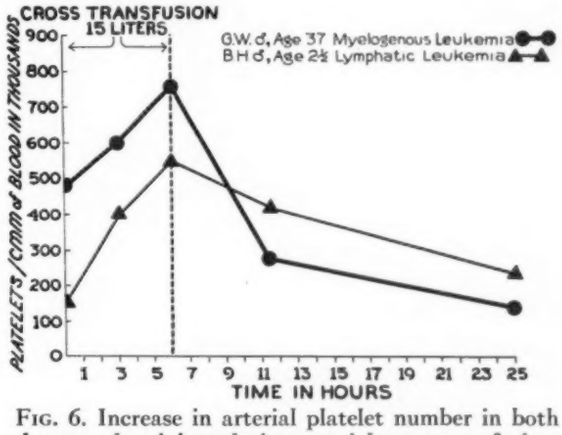

CROSS TRANSFUSION
15 LITERS
G.W. ♂, Age 37 Myelogenous Leukemia
B.H. ♂, Age 2½ Lymphatic Leukemia
PLATELETS / CMM of BLOOD IN THOUSANDS
TIME IN HOURS

FIG. 6. Increase in arterial platelet number in both donor and recipient during arterial cross transfusion.

When the effects of intra-arterially administered epinephrine on splenic vessels were studied arteriographically, the splenic artery exhibited marked contraction shortly after it arose from the celiac artery.[59] There was an absence of the normal small vessel pattern commonly seen without epinephrine. It would appear, therefore, that the flow of blood to the spleen had been markedly decreased or occluded at the point of constriction within ten

to thirty seconds after epinephrine administration which persisted for one to two minutes.

The spleen of dogs and cats and man have been observed to decrease in size following epinephrine administration intravenously or intra-arterially,[2,56,62] but there is little evidence that this decrease in size in man is actually caused by active contraction of the capsule. The human spleen is provided with a fibro-elastic coat (tunica albuginea) which gives off numerous small fibrous bands or trabeculae in all directions, and which upon uniting constitute the framework of the spleen. This fibro-elastic coat, the sheaths of the vessels and the trabeculae are composed of elastic fibrous tissue. There is a small amount of non-striped muscular fibers in man, but in negligible amounts compared to the dog and other animals. It is stated that the distribution of these muscle fibers throughout the spleen explains how the spleen can so quickly alter its volume, but the data for such a conclusion is based almost exclusively upon studies in the dog.[2] The amount of muscular tissue in the human spleen is not sufficient to cause the marked shrinkage of the spleen size observed following epinephrine. A more likely explanation appears to be an epinephrine-induced rise in arterial blood pressure accompanied by spasm of the splenic artery, resulting in decreased arterial blood flow to the spleen with emptying of the vascular bed through the venous channels, thus depleting the spleen of blood which is accompanied by a decrease in size of the spleen. The role of active capsular contraction appears to be minor in man.

Anoxia causes an increase in number of circulating platelets and a decrease in coagulation time. Asphyxia in kittens is also accompanied by thrombocytosis.[63] While it has been suggested that this increase is due to anoxic stimulation of megakaryocytic production in the marrow, which may be so in chronic hypoxia, the prompt and marked increases that are observed following the inception of acute hypoxia occur too rapidly for such a mechanism. In all probability there are at least two mechanisms operating under the conditions of anoxia—one for the acute changes and one for the slower, more chronic varieties.

EVIDENCE FOR BIOCHEMICAL FUNCTION OF THE LUNG IN HEMATOLOGY

Protbrombin. Plasma prothrombin concentration is less in the left ventricle than in the right ventricle of dogs.[64] Arteriovenous sampling of the head, liver, spleen, intestine, kidney and hind limbs shows no significant differences. This decrease in plasma prothrombin content during passage through the pulmonary capillaries has been attributed to platelet production in the lungs as suggested by Howell and Donahue. The reasoning behind this conclusion is that the disintegration of platelets releases thromboplastin which, in the presence of calcium, changes prothrombin to thrombin. This suggestion would appear to implicate platelet breakdown in the lungs equally with platelet formation.

Iron Storage. Iron given intravenously is taken up by the lungs in large quantities initially and then is gradually released to other sites such as the spleen and liver.[65]

Histamine and Histaminase. The histamine content of granulocytic leukemic blood has been shown to reach levels up to 2.3 mg. per 100 cc.[66] Code found that the granulocyte contained the major portion of the histamine in the blood and also noted that the platelet layer occasionally contained histamine. This was also reported by Thiersch.[67] Code attributed the histamine content of platelets to contamination from the granulocytes, but the histamine content of the platelet could also be an inherent characteristic if it were a fragment of the myeloid cell.[25] The lung contains large quantities of histamine and histaminase. Since the hematologic effects of histamine are focused in the lung, the importance of histaminase in the different responses observed in the leukemic and non-leukemic patients bears consideration. Despite the extremely high histamine content of the leukocytes in granulocytic leukemia, the plasma content is negligible. This is evidence against intravascular destruction of leukocytes or the prompt destruction and binding of the released histamine or inactivation perhaps by histaminase.

The lung may serve as a portal of entry of water into the circulation. The hemolysis and hemoglobinuria that follows drowning, if the patient survives, further endangers the subject. In fresh water drowning the contents of the left ventricle are dilute, while in salt water drowning the reverse is true. The exact mechanism of transport of water across the alveolar and capillary wall is obscure.[68]

The lung may act as a route of excretion of leukocytes via the alveoli and sputum. The

alveoli of the lung usually contain granulocytes which appear to be intact, yet there are numerous other cells which are in various stages of disrepair. Interestingly enough the sputum of patients with lymphocytic leukemia contains large numbers of granulocytes with few granulocytes in the peripheral blood.

The capability of the lungs as an excretory channel is great, but little is known regarding the permeability of the pulmonary capillaries, alveolar walls and other membranes for the transport of substances other than the usual respiratory gaseous components.

SUMMARY

The pulmonary circulation is involved in the hematologic system as a portal of entry for stimulating and noxious gases. The erythrocytes, leukocytes and platelets are all involved in the dynamic physiology of the pulmonary circulation. The lungs may also act as a prodigious and facile reservoir for leukocytes and platelets and, under specific circumstances, both for the withdrawal of these elements from the circulation or for prompt delivery into the circulation. The lungs apparently are involved in the production of platelets as well as in their storage. The mechanisms whereby these changes are induced remain to be clarified.

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The Diagnosis of Bronchopulmonary Disease

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IT is the purpose of this article to catalog and discuss briefly those clinical and laboratory procedures which, if applied intelligently, will help establish accurately and rapidly the correct diagnosis of bronchopulmonary disease (BPD). No effort will be made to evaluate the relative importance of the various procedures recommended. The value of any diagnostic procedure depends upon its timely utilization, correct interpretation and proper integration with the total clinical picture. During the past two decades encouraging progress has been made in the surgical and medical management of acute and chronic BPD. Through an intelligent and prompt utilization of new and perfected technics and measures, we are now able to offer favorable prognosis for survival and possible cure in many bronchopulmonary (BP) illnesses which were previously considered inevitably fatal, or which doomed a patient to chronic invalidism and eventual death. Unwarranted delay, unfortunately, or actual failure to establish the correct diagnosis may deprive patients of the benefits of successful therapeutic intervention in remedial conditions. It is true, however, that on occasion even the most astute clinician is unable to solve some of the more difficult diagnostic problems following careful study. This situation is to be expected and excused. There is, however, no apology for ignorance of, or failure to utilize, all existing and available clinical and laboratory diagnostic aids in conducting an investigation of a BP complaint.

DIAGNOSTIC METHODS

History and Physical Examination

Routine History. This should consist of the following: (1) chief complaint, (2) history of present illness, (3) system review, (4) past history, (5) family history, (6) marital history, (7) social history. Logical investigation of each case should begin with a brief, clear statement of the patient's chief complaint followed by a detailed and accurate history obtained in a friendly and leisurely manner in the sequence outlined. The final recorded history should be an integrated, simple word-picture of the information supplied spontaneously by the patient and to which has been added the examiner's objective observations. Each symptom requires careful evaluation. The differential characteristics of those which are especially referable to the lungs deserve painstaking study and correlated interpretation. Particular emphasis should be placed on such symptoms and observations as cough, sputum, hemoptysis, dyspnea, orthopnea, wheezing, cyanosis, pain in the chest, hoarseness, fever, chills, loss of weight, nature of onset and progress of the illness, seasonal, diurnal, climatic and geographic variations, relation to previous illness and method of obtaining relief. These symptoms and observations when present require careful quantitative and qualitative evaluation of their characteristics so that to each may be assigned its relative significance. For example, the symptom of cough will have no significant value unless analyzed carefully and its special characteristics assessed properly. The differential characteristics of each symptom and observation should be evaluated with diligence. In this manner the correct diagnosis may be suspected, or established, while the integrated history of the present illness is being recorded. The history of the present illness should not be recorded in final form until the physician has conducted a detailed system review. This practice provides an opportunity for the examiner to seek the answers to questions which may develop

additional pertinent facts or re-emphasize the significance of previously obtained information. The patient's negative or affirmative reply to a simple routine question in the system review, which on the surface seems entirely unrelated to the respiratory organs, may frequently supply the clue in a difficult diagnostic problem.

Frequently the existence of acute or chronic BPD masquerades behind a curtain of bizarre symptoms. In these circumstances the most experienced examiner may be misled and remain ignorant of the true nature of the disease even after the history of the present illness and system review have been elicited. This information may be clarified, or the correct diagnosis suspected, while obtaining the past history. Pulmonary tuberculosis, bronchiectasis and other chronic BP diseases such as fungus infections may be suggested by a past history of recurrent or frequent pleurisy, atypical pneumonia, periodic loss of weight and energy without obvious reasons, recurrent bouts of fever and night sweats of undetermined origin. The recent history of an operative procedure such as a tonsillectomy, tooth extraction or any infection of the mouth, tonsils, nasal or oral pharynx may focus attention on the possibility of a lung abscess. A history of amebic dysentery in the past may actually suggest the etiologic agent responsible for the abscess. Pulmonary embolism, infarction and metastatic abscesses may be suspected if the examiner obtains a history of phlebothrombosis, thrombophlebitis, recent fracture or severe localized or systemic infection. The history of a childhood illness complicated in its convalescent stage by pneumonia or a prolonged cough should invite consideration of bronchiectasis as a diagnostic possibility. Pulmonary abscess, bronchiectasis and chronic pneumonitis should be considered when one elicits a history of esophageal stricture, carcinoma, cardiospasm, chronic alcoholism, general debility, recent general anesthesia or coma. History of the prolonged use of oily nose drops and oily cathartics requires the inclusion of lipoid pneumonia in the differential diagnosis. Recent intense radiation therapy of a lesion in the region of the thorax should lead one to suspect radiation pneumonitis. This complication is especially frequent following roentgen ray therapy for carcinoma of the breast. History of chronic renal failure should invite consideration of uremic pneumonitis. These are but a few examples of the obvious value of a carefully obtained past history.

The strictly personal elements in a patient's history frequently acquire added significance when interpreted in the light of the family and marital history. This is especially true of contagious diseases such as pneumonia and tuberculosis or when a hereditary tendency is uncovered to support the possible diagnosis of asthma or cancer. In obtaining the family history the examiner should not accept unequivocally the patient's diagnosis of familial illnesses. He should attempt to confirm all diagnoses supplied by the patient, especially those which may influence his ultimate decision. This objective may be attained by ascertaining and evaluating the signs and symptoms personally or by obtaining the information directly from the physician who established the diagnosis in question. Unless extreme caution is exercised in this respect, many serious errors will be committed. Investigation of every diagnosis in this fashion will prove many to be misleading and still others to be completely erroneous. Similarly, patients frequently attempt to conceal confirmed diagnoses in order to avoid what they consider a social onus. This is especially true of pulmonary tuberculosis.

Finally, the examiner should obtain the patient's social history. Such diseases as silicosis, asbestosis, byssinosis, pneumoconiosis of soft-coal workers, bagassosis, Shaver's disease, diatomaceous earth pneumoconiosis and arc-welder's disease may be suspected from the patient's occupational history. Geographic location may necessitate consideration of coccidioidomycosis, histoplasmosis, echinococcal disease and other less common conditions. Psittacosis should be included in the differential diagnosis of patients exposed to members of the parrot family, pigeons and other fowl known to harbor the responsible virus. In general, all personal habits which may be of significance in the final evaluation of the case should be noted carefully.

An orderly, correlated history obtained in this fashion will suggest the diagnosis in many instances before the physical examination or any other procedures are completed. In a substantial number of cases, however, the examiner will be distressed at the apparent lack of assistance gained from even the most

assiduously recorded history. No matter how often this unfortunate situation occurs, the physician must never consciously lower the recognized standards of a satisfactory history. As it so often happens, the first manifestation of carelessness will be rewarded by a missed diagnosis. Those of us who have experienced this misfortune will never again be satisfied with an abbreviated record of a patient's illness. The apparent bonanzas of diagnostic short cuts have a notorious habit of backfiring at the wrong time to the complete embarrassment of the would-be beneficiaries and to the detriment of the unfortunate patient. This latter observation applies with equal significance to all elements of the patient's examination; history, physical and laboratory. The physician, not the clerical helper or nurse, should obtain the history.

Physical Examination. Physical examination of the patient suspected of suffering from BPD must be performed in each case. No matter how incontrovertibly the evidence in the patient's history points to a specific BPD, omission of the slightest detail in the physical examination is fraught with danger. In general, the physical findings will confirm, or disprove, the impressions gained from the patient's clinical history. Quite often a routine examination will reveal significant physical findings in an organ, or organs, other than the one to which the history has directed the examiner's attention. Imagine the physician's surprise when a disease process is located in the left lower lobe of the lung of a patient complaining of anorexia, nausea, vomiting and epigastric pain. In this, and similar circumstances, the examiner will find it necessary to supplement the original history with new and added information obtained by re-interrogation of the patient. A majority of diseases involving the lung are localized to that organ, but a significant minority are merely reflections of a remote or systemic disorder. This very fact again emphasizes the necessity of a complete physical examination even in those instances which do not appear to warrant detailed study. Discovery of phlebothrombosis or thrombophlebitis in an extremity will establish an etiologic background for pulmonary embolism or infarction. It will also facilitate the institution of proper prophylactic measures to avoid further possibly fatal accidents. Dependent edema, venous engorgement and tender hepatic enlargement will incriminate the heart as the responsible organ rather than the lungs in a patient complaining of cough, blood-tinged sputum and dyspnea. Observations obtained by physical examination in such instances facilitate evaluation and correlation of the clinical history. A distant lymph node, a draining sinus, a skin lesion or an enlarged prostate may be significant when examined histopathologically or bacteriologically. Clubbing of the fingers and toes may lead to a suspicion and subsequent confirmation of existing BPD.

Clinical and Laboratory Aids

When the history and physical examination are complete and correlated, the diagnosis is often apparent. There are, however, a significant number of BP diseases which can be diagnosed only with the assistance of routine and highly specialized clinical and laboratory diagnostic procedures. Familiarity with all of these procedures is an essential part of the armamentarium of those physicians specializing in diseases of the chest. These methods, however, should be equally familiar to all engaged in the practice of medicine and its various specialties. Knowledge of these procedures will enable the physician to establish a diagnosis with greater frequency, rapidity and accuracy. Additionally, realization of his own limitations will prompt him to offer the patient the advantages of more specialized consultation study if indicated. In general, all of the following diagnostic measures should be considered as secondary aids to be utilized only after a complete history has been obtained and a thorough physical examination has been performed.

Hematologic Studies. Hematologic studies are frequently of assistance but are rarely of significance in diagnosing BPD. A normal red count or one manifesting some degree of anemia is of no particular importance. Polycythemia, on the other hand, is a significant laboratory finding since it may be responsible for BPD which was not suspected before examination of the blood. Erythrocytosis, when associated with pulmonary disease, usually signifies chronic oxygen lack. It may accompany such clinical entities as Ayerza's disease, emphysema, far advanced cystic disease or any other condition interfering with adequate oxygenation of the red cells. Erythro-

cytosis is a rather constant finding in pulmonary hemangioma (arteriovenous fistula). Erythremia, or polycythemia vera, is commonly accompanied by pulmonary signs and symptoms. The total white blood count and differential characteristics are useful in determining the existence and type of infection. For example, one may expect a normal total white blood count with primary atypical pneumonia of undetermined etiology. A definite leukocytosis, however, with a left shift is typical of pneumococcic pneumonia. The total white blood count and differential generally contribute only limited assistance in helping to establish specific diagnoses in BPD. It is true, nevertheless, that the finding of an eosinophilia may be the first clue in such diseases as Loeffler's syndrome, Hodgkin's disease or echinococcal disease involving the lungs. Some degree of eosinophilia has been reported in silicosis, but the author does not believe that the total white blood count or differential is of particular diagnostic significance in this disease entity or in tuberculosis. When leukemic processes involve the pulmonary tissue, the total white blood count and differential are helpful. Aside from Hodgkin's disease, a study of the white blood cells does not contribute much to the diagnosis or evaluation of the other lymphomas. Although it is true that the routine hematologic study of a patient is not commonly decisive in the ultimate evaluation and diagnosis of BPD, it should never be omitted. It may occasionally be helpful and practically diagnostic. Also, it should be remembered that a rising or falling total white blood count and a shifting Schilling hemogram have the same prognostic value in BP infections as they do in other infectious diseases.

Examination of the Urine. Although the author does not recall a single instance of BPD in which this examination was diagnostic, it should, nevertheless, continue to be a routine laboratory procedure because of its value in considering the differential diagnosis.

Stool Examination. In Loeffler's syndrome the discovery of Strongyloides stercoralis, Ascaris lumbricoides, Necator americanus or other ova in the stool is of great assistance. When Endamoeba histolytica cysts or trophozoites are found in the feces, the etiology of a lung abscess may be suspected and subsequently proved. These are but a few examples in which examination of the stool for parasites may yield important diagnostic information. The detection of occult blood in the stool may reveal the source of pulmonary metastasis.

Serologic Test for Syphilis. Rarely is this test of any diagnostic significance in BPD.

Sputum Examination. This is one of the most reliable and important procedures and should be utilized routinely in every case of undiagnosed BPD. Suitable specimens for examination may be obtained from ordinary expectorated material. When the amount of sputum raised is insufficient or unsatisfactory, material for examination may be obtained by pulmonary lavage or bronchoscopic aspiration of the trachea and accessible bronchi. Microscopic examination of appropriately stained smears should be performed in a search for the responsible pathogen. One should not be content with one, two or even three negative results if strong clinical evidence exists which incriminates the lungs and points to a certain disease. Repeated careful examinations are mandatory when tuberculosis is suspected. A concentrated twenty-four hour sputum specimen is the procedure of choice. The type of stain employed is a matter of individual preference. If the usual staining technic fails to reveal the organism, then the sputum should be cultured on appropriate media. Fresh unstained material should be examined when attempting to identify the trophozoites of E. histolytica. An unstained specimen mixed with either a 10 per cent solution of potassium hydroxide or sodium hydroxide is also the procedure of choice when a fungus infection is being considered. When echinococcal disease of the lungs is suspected, the diagnosis may be established by identification of the hooklets or membrane of the cyst in a properly stained specimen. Since the advent of effective antibiotic therapy, sputum typing is no longer as important as previously in lobar or bronchopneumonia.

If sputum examination would end with a search for the responsible pathogenic microorganism, it would be incomplete. The gross and other stained and unstained microscopic characteristics of the BP excreta must be studied in order to secure the maximum diagnostic benefits from this source. Identification of fat globules will in itself confirm or suggest the diagnosis of lipoid pneumonia. Loeffler's syndrome or asthma may be suspected when the predominating cellular elements are eosino-

phils. Identification of elastic fibrils and Charcot-Leyden crystals make the latter possibility more probable. The recognition of larvae of A. lumbricoides indicates an ascaris pneumonitis. If bronchogenic carcinoma is suspected, properly prepared specimens should be examined for cancer cells.

The gross characteristics of the sputum must be studied carefully as this part of the examination frequently suggests the diagnosis. For example, a frothy, rust-colored sputum, with or without bloodstreaking, invites a diagnosis of pulmonary edema while a three-layered sputum is suggestive of bronchiectasis. Pulmonary tuberculosis, bronchiectasis and neoplasm are among the diagnoses to be considered in the presence of varying degrees of hemoptysis. Foul-smelling sputum should make one suspect lung abscess or bronchiectasis. Prune juice–colored expectoration may signify lobar pneumonia while amebic abscess of the lung may be characterized by sputum with the appearance of anchovy sauce. When the gross characteristics of the sputum are similar to fluid obtained by thoracentesis, a bronchopleural fistula is likely. Accidental discovery of a broncholith may be the answer to a difficult diagnostic problem. Characteristic sulfur granules mean actinomycosis while the presence of Curschmann's spirals and Laennec's pearls are suggestive of asthma. Determination of the twenty-four hour sputum volume is very helpful in suspected cases of bronchiectasis, pulmonary abscess and bronchopleural fistula.

Gastric Contents. This method of study should be employed whenever the bacteriologic results of sputum examination by stain and culture are consistently negative while all clinical evidence, nevertheless, is to the contrary. It is frequently the only method of establishing the diagnosis. The results of guinea pig inoculation will decide the significance of acid-fast bacilli recovered from gastric washings. Pathogenicity of the organism may be determined in this fashion. Examination of fasting gastric contents is especially valuable in attempting to establish a diagnosis of pulmonary tuberculosis in the aged, the debilitated and in very young children.

Blood Cultures. Early in the course of lobar or bronchopneumonia, and before a chemotherapeutic or antibiotic agent has been employed, the blood culture may be positive. Isolation of the responsible organism in the blood stream is confirmatory but not diagnostic. Blood cultures are generally of limited value in the diagnosis of BPD. The results of this study, however, influences the prognosis.

Skin Tests. In many obscure BP conditions the diagnosis may be suggested by the nature of the patient's response to a measured, minute skin test dose of antigen obtained from a specific microorganism. This test is especially valuable in such diseases as tuberculosis, coccidioidomycosis, blastomycosis, histoplasmosis and other fungus diseases. In some instances a negative result, however, is of far more clinical significance than a positive reaction. Physicians should be thoroughly familiar with the correct technic of performing the test and the criteria for proper interpretation. When echinococcal disease of the lungs is suspected, Casoni's intradermal test is specific. All asthmatics should be tested for possible allergic response to suspicious antigens both for diagnostic purposes and therapeutic potentialities.

Sedimentation Rate. For many years this determination has been practically a routine procedure in the study of some chronic pulmonary diseases. Its popularity far exceeds its diagnostic value, but may be attributed to its questionable prognostic significance and ease of accomplishment. It is a non-specific laboratory test of limited value which should be interpreted only in the light of the total clinical and laboratory picture.

Precipitin and Complement-fixation Tests. These procedures are valuable in the diagnosis of virus and fungus diseases. When significant positive results are obtained, they may be considered diagnostic. In some instances, as for example in blastomycosis and coccidioidomycosis, a rising or falling titer is of prognostic as well as diagnostic value.

Roentgenologic Examination. No examination of the lungs is complete without roentgenologic study of the chest. An erect, postero-anterior view should be a routine procedure for all patients suspected of having BPD. A good lateral view of the chest may be as important as the postero-anterior examination. In some clinics it is a routine procedure. Frequently lesions are recognized on the lateral view which are not even suspected after the most careful interpretation of the postero-anterior film. Economic considerations permitting, and if time, equipment and personnel are available, the lateral view should be routine

in the diagnosis of BPD. Roentgenologic examination of the lungs is unquestionably one of the most valuable of all diagnostic procedures but under no circumstances should it be considered a substitute for the routine history and physical examination. The value of a chest roentgenogram may be realized only if its significance is made contingent on the history, physical examination and other clinical and laboratory procedures. Although roentgenographic examination of the chest is of tremendous importance in the diagnosis of BPD, it may be overemphasized. By itself it is rarely diagnostic. Generally, a chest roentgenogram underestimates the amount and extent of actual pulmonary disorder. It does, however, permit early detection of silent and unsuspected lesions and is essential for careful follow-up examination. Therein lies its greatest contribution to the study of BPD. Serial roentgenograms are excellent prognostic guides. On occasion, the results of physical examination of the lungs are more informative than the roentgenogram. More frequently, however, the roentgenogram will reveal a BP lesion even after the most competent diagnostician has rendered a negative opinion based on physical examination. This unfortunate shortcoming of physical diagnosis in the recognition of BPD may be overcome through increased utilization of routine roentgenographic examination of the lungs. Equipment and supplies for mass radiographic campaigns are now becoming increasingly available and the cost is so nominal that even economic considerations are no longer of consequence.

The following roentgenologic studies of the lungs are valuable diagnostic procedures: (1) erect, postero-anterior; (2) lateral; (3) oblique; (4) lordotic; (5) stereoscopic; (6) planographic; (7) kymographic; (8) bucky film; (9) lateral decubitus; (10) spot film; (11) maximum inspiration and expiration. Any of these studies, and especially the more difficult technical procedures, should be undertaken and interpreted only by physicians qualified to engage in the practice of roentgenology or diseases of the chest. Adequate study of BPD depends on roentgenographic examination and interpretation. It is mandatory for chest physicians to be competent roentgenologists as far as the thorax is concerned. Occasionally, study of any part of the gastrointestinal tract with a radiopaque substance may be indicated because of differential diagnostic considerations. This is especially true in diaphragmatic hernias and diseases of the esophagus. Roentgenographic examination of other parts of the body may also be indicated under certain circumstances. If the pulmonary lesion appears to be metastatic, one is obliged to investigate all possible primary sites.

Fluoroscopy. This study of the lungs is very valuable in determining mobility and other dynamic features of the chest during various phases of respiration. One may study and estimate the functional activity of each lung in this manner by observing the density changes during various phases of respiration together with the movement of the ribs, the mediastinal structures and excursion of the diaphragm. Fluoroscopic determination of diaphragmatic excursion is more reliable and preferable to radiographic study. Aneurysms may be diagnosed from their expansile nature and so differentiated from solid tumors. The Valsalva maneuver may be utilized to advantage in studying aneurysms. Fluoroscopy is valuable in such conditions as pneumothorax and pleural effusion. It is not a substitute for a satisfactory radiograph of the lungs. Many lesions escape detection by even the most competent fluoroscopist if sole reliance is placed on this method of examination. However, when it is necessary to consider the gastrointestinal tract in the differential diagnosis of BPD, fluoroscopic examination may be more reliable than the roentgenogram.

Examination of Pleural Fluid and Gases. Whenever the presence of a pleural effusion is confirmed, a specimen must be obtained for diagnostic purposes as soon as possible. Unless specifically indicated, air should not be introduced into the pleural cavity during or following diagnostic aspiration. Part of the fluid obtained should be consigned for bacteriologic examination. If a specific diagnosis is suspected, special stains, cultures and other bacteriologic studies should be ordered. For example, if one suspects a tuberculous effusion, then a guinea pig inoculation is indicated. Fluid which has developed synpneumonically, or metapneumonically, should be examined for pneumococci. If one suspects a malignancy, part of the specimen should be examined histopathologically for neoplastic elements. The type of leukocyte, if present, can be determined from a stained smear while searching for

pathogenic bacteria. In this way the inflammatory nature of an effusion may be detected. Sufficient fluid should be obtained to determine the specific gravity or protein content. These examinations are valuable in differentiating an exudate from a transudate. Before withdrawing the aspirating needle, 10 cc. of 1 per cent methylene blue, or some other suitable dye, may be instilled if a bronchopleural fistula is suspected. In the presence of this complication the sputum will have a bluish discoloration within twelve to twenty-four hours, or sooner, following injection. This is a very valuable diagnostic aid which offers incontrovertible evidence when positive. Where facilities for gas analyses are available, the existence of a bronchopleural fistula may be suggested by determination of the carbon dioxide and oxygen content of gas obtained from the pleural cavity. This time-consuming procedure is usually unnecessary and merely of academic interest.

Macroscopic examination of the fluid obtained by thoracentesis is not a very reliable procedure, but odor, viscosity and color may suggest certain diagnostic possibilities and additional methods of study. For example, a pale straw-colored fluid obtained from the right hemithorax may suggest congestive failure with hydrothorax. Milky, thin fluid invites a diagnosis of chylothorax which may be confirmed by staining with Sudan III and chemical analysis of its fat content. A blood-tinged, or frankly bloody, fluid suggests pulmonary infarction, trauma, congestive heart failure, tuberculosis, pulmonary or pleural neoplasm and other possibilities. Foul-smelling fluid may suggest an anaerobic infection or a colon bacillus. From this brief discussion the diagnostic importance of fluid in the pleural cavity should be obvious. The examiner must be prepared to obtain every possible assistance from the complete investigation of this easily available pathologic material.

Endoscopic Studies. Bronchoscopy is not employed with sufficient frequency in the diagnosis of BPD. Yet, it affords the clinician a possible opportunity to visualize the lesion directly. Material for bacteriologic and histopathologic examination may be obtained in this manner. The appearance of some lesions is almost diagnostic. In any unexplained BPD this examination should be performed without procrastination as it is relatively harmless. The physician should not hesitate to submit his patient to this examination for the expected benefits are far more numerous than the possible dangers. Bronchoscopic examination should be considered in all cases of obscure and atypical BP lesions. In this way more cases of BP cancer will be discovered in an operable and possibly remedial stage.

Esophagoscopy may be a very valuable procedure in differentiating between esophageal disease and BPD. Frequently esophageal disease is discovered to account for secondary BP complications as in stricture and carcinoma of the esophagus, or cardiospasm.

Bronchography. The introduction of a radiopaque substance into the tracheobronchial tree is a simple, usually safe and valuable diagnostic procedure. A history of sensitivity to iodine, however, precludes its use. It is of unparalleled value in patients suspected of having bronchiectasis and may also be employed to demonstrate bronchial occlusions, cystic disease and pulmonary cavitation. The method of choice in carrying out this examination is one of individual preference. Following instillation of a suitable radiopaque solution into the tracheobronchial tree, immediate fluoroscopic and indicated roentgenographic examination should be performed.

Miscellaneous Uses of Radiopaque Material. When a sinus tract appears to communicate with the lung or the pleural cavity, a radiopaque solution may be used to outline the tract and to localize the communication. In positive instances the radiopaque material can be demonstrated in the lungs fluoroscopically and roentgenologically. This procedure is especially useful in thoraco-abdominal actinomycosis with sinus tracts.

Biopsy of Lesion for Histopathologic and Bacteriologic Study. When a diagnosis cannot be established by sputum examinations or other simple laboratory techniques, biopsy of available pathologic material may be performed. The tissue should then be examined by the proper histopathologic and bacteriologic methods. Material for biopsy may be obtained from the local pulmonic lesion or from other sites if the BPD is part of a systemic illness. Suitable specimens may be obtained bronchoscopically. Bronchial adenomas have a tendency to bleed freely following biopsy. This is only a minor complication and should not be considered a contraindication to the pro-

cedure. The bronchoscopist must be well oriented before securing the biopsy specimen and is required, before the operative procedure is undertaken to determine carefully the possible existence of a thoracic aneurysm. Accidental biopsy of the aorta or other great vessels may be a rather embarrassing complication. When material for biopsy is bronchoscopically inaccessible, the author has unhesitatingly performed innumerable punch biopsies of pulmonary lesions situated at respectable distances from vital structures. If a Vim-Silverman biopsy needle is used, sufficient material of diagnostic quality may be obtained without any more serious sequelae than transient blood-spitting. The advisability of punch biopsy in suspected malignancies, nevertheless, remains controversial. Aspiration biopsy is not as satisfactory since material obtained in this fashion is usually insufficient for adequate histopathologic examination although it is quite frequently suitable for bacteriologic study. When pulmonary tissue is not available for histopathologic or bacteriologic examination or has been found non-diagnostic, other accessible sites should be considered. In such instances one may conceivably establish the diagnosis from a lymph node, skin lesion, draining sinus or from any other suitable site. If it appears that the pulmonary disease represents a metastatic lesion, biopsy of the original focus is preferable. Suspected leukemic infiltrations of the lung may be confirmed by aspiration or biopsy of the sternal bone marrow in addition to examination of the peripheral blood. When the possibility of a fungus infecton is being considered, a Hotchkiss-McManus stain should be used. Histopathologic and bacteriologic examination of tissue obtained by biopsy is a reliable method of establishing an etiologic diagnosis quickly and irrefutably.

Diagnostic Pneumothorax and Pneumoperitoneum. Pneumothorax is an excellent method of distinguishing between pulmonary and extrapulmonary lesions. Pneumoperitoneum has little place in the diagnosis of BPD unless diagnostic pneumothorax fails to reveal the exact location of a lesion in the region of the diaphragm.

Thoracoscopic Examination. After a diagnostic pneumothorax has been established, it is a relatively minor surgical procedure to examine the contents of the pleural cavity with the thoracoscope. This sometimes permits direct visualization of the lesion for purposes of surgical evaluation and diagnosis. Biopsy specimens may be obtained in this manner for histopathologic and bacteriologic examination.

Electrocardiogram. This procedure has only limited value in the diagnosis of BP diseases. As in the case of cor pulmonale it may reflect cardiac and pericardial complications secondary to the BPD. If the investigation, however, has been conducted correctly and in logical sequence, the information obtained from the electrocardiogram will be of confirmatory rather than diagnostic importance. When the differential diagnosis rests between pulmonary embolism and coronary occlusion, however, it is diagnostic. Low voltage in the presence of massive pleural effusion is only of academic interest.

Venous Pressure and Circulation Time. Venous pressure and circulation time determinations are of definite value in helping to differentiate between cardiac disease and BPD. In the presence of cardiac failure the venous pressure is elevated commonly. This is not usually the case in BPD. On occasion, primary or metastatic tumors in the thorax will obstruct the venous return from one part of the body or another but not symmetrically as one would expect in cardiac decompensation. This latter observation together with other available evidence, such as collateral circulation, will usually decide the issue.

Determination of the circulation time in BPD is of questionable value. In chronic fibrotic diseases of the lung associated with dyspnea the circulation time is frequently accelerated. A prolonged circulation time is a more constant characteristic of cardiac decompensation than uncomplicated BPD.

Therapeutic Test Dose of Deep Roentgen Ray Therapy. If a BP lesion remains undiagnosed after all available diagnostic procedures have been utilized, then a test dose of deep roentgen ray therapy is indicated. Response to this form of therapy is very striking in lymphoblastomas. It has therapeutic and diagnostic possibilities.

Angiocardiography. An intravenous or intracardiac injection of a radiopaque substance will frequently differentiate vascular tumors of the thorax from other pulmonary lesions. It may also be used to help outline non-vascular tumors. The diagnosis of pulmonary arterio-

venous fistula can be established by this examination. It is not without danger, however, and requires highly trained, technical assistance and rather involved apparatus. Therefore, it is not recommended as a routine procedure. Iodine sensitivity must be considered as in bronchography.

Exploratory Thoracotomy. If all other examinations are non-diagnostic, the physician is justified in recommending exploratory thoracotomy in properly selected cases. When BP malignancy is suspected, exploratory thoracotomy should not be delayed. In the hands of a competent thoracic surgeon this procedure carries no greater risk than an exploratory laparotomy and may eventuate in a cure.

Physiologic Studies of Pulmonary Function. Pulmonary function studies in general have little diagnostic value in the study of BPD. However, indicated studies to determine pulmonary ventilation and diffusion are important in evaluating the functional status of the lungs. Cardiac and pulmonary catheterization have diagnostic and prognostic value.

Radioactive Isotopes. Administration of radioactive iodine may be used to confirm the existence of pulmonary metastases from carcinoma of the thyroid. To date there is no record of other radioactive substances being used in the diagnosis of BPD.

COMMENTS

Some BP diseases may be encountered which will require the supplementary utilization of other indicated and highly specialized procedures in order to establish the correct diagnosis. For example, gastroscopic examination, determination of the alkaline phosphatase blood level or a retrograde pyelogram may be necessary in some instances. To enumerate and discuss all these possibilities would be an almost impossible assignment.

As a rule, orderly investigation and intelligent utilization, correct interpretation and careful selection of indicated clinical and laboratory procedures enumerated herein will be rewarded by a prompt and accurate diagnosis of existing BPD.

To render a patient the best possible service, the physician must be thoroughly familiar with and willing to practice the proper and acceptable methods of orderly investigation. Sincere cooperation between the internist, surgeon, radiologist, pathologist and possibly other specialists is also imperative in the diagnosis of BPD.

Bacterial Examination of the Sputum in Pulmonary Disease

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In the diagnosis and treatment of pulmonary disease the clinical, roentgenologic and bacteriologic findings must be considered and correlated. All of these methods are important, with the sputum examination of decisive significance in the management of pulmonary disease. In this discussion the first section will be devoted to sputum findings in chronic pulmonary tuberculosis, and non-tuberculous pulmonary conditions will then be reviewed.

Chronic Pulmonary Tuberculosis. The presence of tubercle bacilli in sputum has important diagnostic, therapeutic and prognostic implications. The absolute diagnosis in cases of pulmonary infiltration of undetermined etiology, the evaluation of the activity or clinical significance of known tuberculous lesions, the indications for treatment and appraisal of the effectiveness of the therapeutic measures are all related to the bacteriologic findings.

In the search for tubercle bacilli the method of examination can vary. Included in the different means of diagnosis are the direct smear, concentration, culture and guinea pig inoculation. The daily output of tubercle bacilli will determine the sensitiveness of these bacteriologic methods. The ascending order of sensitivity in the detection of tuberculosis is as follows —the direct smear, concentration of sputum or fasting gastric contents, culture of sputum or gastric contents and guinea pig inoculation.

In practice, as one method proves negative, the next more sensitive test is done to find the tubercle bacilli. The direct smear is of little value except as an immediate indication if positive that there is a very high output of bacilli and heavily infected sputum. Routinely all of our sputum specimens are concentrated, for this will reveal many more bacilli than a direct smear. If the concentrates are negative or there is little or no expectoration (or an unsatisfactory specimen—nasopharyngeal material), fasting gastric contents are examined. The yield of positive results from examination of gastric concentrates is small and under 5 per cent, and therefore, except for special cases, all of our gastric specimens are routinely cultured. With good culture technic even a few bacilli will be demonstrated. If gastric and sputum cultures are negative, the final (and most conclusive) method of finding tubercle bacilli would be by guinea pig inoculation.

The incidence of positive sputum reports will vary directly with the time used for the collection of the sputum. The longer the interval for accumulation of sputum, the higher the number of positives. The routine collection is for a forty-eight-hour period, and in special circumstances three or four days and sometimes more are allowed.

When the specimen is being collected, all expectoration must be included irrespective of its appearance. The patient should be advised to expectorate and not swallow sputum. There is no characteristic gross appearance to differentiate the sputum in tuberculosis from other pulmonary conditions. Mucopurulent secretions are most common but a sputum that is mucoid or bloody may also be positive. Even in the presence of frank hemoptysis the sputum specimen can be positive for tubercle bacilli. Tuberculous cavitation is usually associated with a heavy purulent sputum and tubercle bacilli should be found readily in it. A purulent sputum persistently negative has a non-tuberculous etiology which must be determined. Non-tuberculous cavitation can be caused by a pulmonary abscess, bronchiectatic abscess, fungus disease, infected cyst and necrotic neoplasm or infarct.

There is natural variation in the number of bacilli expectorated, and they are not constantly present in every specimen. It is therefore very important in diagnosis to have repeated sputum examinations over a period of time. A valid conclusion about the presence of tuberculosis cannot be made from one or a few negative specimens (smear, concentrate or cul-

ture). However, it is usual in active cases of tuberculosis for the sputum examinations to be positive within a short period of time with early diagnosis possible. On rare occasion after many negative concentrates and cultures and even months of observation, a single culture may be positive. Even in cases with infiltration roentgenologically typical of tuberculosis bacteriologic diagnosis may be delayed. In such instances bronchoscopic aspiration may yield material positive for tuberculosis. In cases of questionable diagnosis, other methods such as laryngeal swabs and tracheobronchial lavage have been used. I have had no experience with these procedures. Laryngeal swabs have been reported to be 72 per cent as effective as gastric aspiration for detecting tubercle bacilli in chest clinic patients.

Not only is it important to have successive examinations of the sputum, but also it is essential to utilize all the different bacteriologic methods in order to have a reliable conclusion in diagnosing tuberculosis. Analyzing any one method of sputum examination will show that with the use of only a single test, many cases are missed that are found positive as the tests are repeated. Although sputum smears and concentrates will reveal a majority of those positive, without the use of gastric aspirations and cultures (and animal inoculations) about 30 to 40 per cent of positive cases would be undiagnosed. In fact if all methods of examination are employed persistently, close to 100 per cent of cases of active pulmonary tuberculosis including those of minimal degree can be found positive.

In comparative studies of guinea pig inoculations and cultures the value of each method and the advantages and disadvantages of their use in finding tubercle bacilli have been described. An adequate amount of material (sediment) prepared properly is required for each test. The more tubes of medium planted with each specimen, the more sensitive the results of the cultures. In some laboratories two guinea pigs are used for each inoculation. Cultures may be lost by contamination and animals may die from different causes before tuberculosis can be diagnosed. Although cultures are kept for at least eight weeks, from 85 to 90 per cent of those positive will show growth within three to five weeks. Guinea pigs are kept six to eight weeks before examined for evidence of tuberculosis. However, by tuberculin-testing the animals (only tuberculin-negative pigs are used) conversion from negative to positive may be noted within three weeks, which is a very important diagnostic consideration. The appearance of palpable lymph glands in the groin of the pig in about three or more weeks is also an early diagnostic sign. Cultures are easy to do while a proper animal set-up requires larger facilities and greater handling cost. Although the most sensitive method of finding tubercle bacilli is by guinea pig inoculation, from a practical point of view, in expert hands, cultures are not much less efficient than animal inoculation. In our hospital laboratory cultures are done routinely and guinea pig inoculation is used only on occasion in special cases for diagnosis and evaluation of therapy.

The value of "gastrics" will depend on the method used to obtain the fasting gastric contents and the rapidity with which the material is examined. It is most desirable to do the aspiration as soon as the patient has awakened. To diminish stomach peristalsis, it is essential for the patient to have nothing by mouth and to rest as much as possible before the test. This will permit evacuation from the stomach of all swallowed sputum. It is most important to have an immediate laboratory examination because with any delay the chances of finding tubercle bacilli will be diminished because of a substance in the stomach juices normally present which inhibits bacillary growth. The exact nature of this inhibitive substance is not known although it has been considered to be the hydrochloric acid or the gastric lipase or pepsin in the presence of the acid. In any case, if there is to be a delay in examination of the gastric contents, then to maintain viable bacilli the specimen should be neutralized and kept refrigerated.

The importance of positive cultures in the handling of pulmonary tuberculosis has not been a settled issue. This matter has been the subject of special study and the main conclusions reached in this investigation will be presented. In these patients all the concentrates were negative and only the cultures were positive. The significance of cultures is related to many factors: (1) frequency of positive reports, (2) type of pulmonary infiltration, (3) roentgenologic changes in the tuberculosis, (4) correlation with collapse procedures or surgical therapy.

The incidence of roentgenologic modifications of any kind (improvement or progression)

is related to the frequency of positive cultures. Thus alteration of the tuberculous lesion is quite rarely associated with a single positive culture; it occurs in a minority of patients with occasional positive reports and takes place in almost every case with a majority of positive cultures.

Correlation of the frequency of positive cultures and prognosis is shown by follow-up studies of patients discharged from the New York City Municipal Sanatorium. Most unsatisfactory results with progression of the lesion, rehospitalization or change from negative to positive sputum occur in patients with positive cultures compared to those with negative findings before discharge. The highest breakdown rate is evident in patients with a majority of positive cultures compared to those with only an occasional or single positive report.

Soft and cavitary pulmonary tuberculous lesions by their very nature will show much roentgenologic change. These modifications are closely correlated with positive cultures. In lesions of a fibroproductive nature there will often be no alteration with an occasional positive but progression can occur when the cultures are persistently positive.

Regression or resolution of pulmonary tuberculosis can occur in the form of absorption of soft infiltrations, closure of cavitation or an increase in fibrosis. These changes can be associated with positive cultures. Roentgenologic improvement of the tuberculosis indicates that the lesion is still unstable or active. When the disease reaches a point of real stability, however, the cultures will become and remain negative.

Progressive tuberculous changes with an increase in the extent of the lesion, the appearance of cavitation or enlargement of preexisting cavities, could be associated with positive cultures. In patients with a majority of cultures positive the most frequent roentgen change was progression.

The importance of positive cultures is emphasized not because of their appearance at the time of actual progression but particularly as they can antedate the roentgenologic findings by many weeks or even months. This warning of impending change in the lesion is of special significance in patients with infiltration of soft or mixed nature, equivocal cavitation or questionable progression. Persistently positive cultures are as significant as positive sputum concentrates in evaluation of the tuberculous picture and therapeutic indications. Positive cultures sometimes even antedate symptoms which may not appear until progression is evident.

There is considerable value in the correlation of cultures with the collapse therapy and surgical procedures used in tuberculosis. In the non-resectional types of treatment (pneumothorax, pneumoperitoneum or thoracoplasty) the cultures usually show a gradual conversion over a period of months until healing is established and then they remain negative. In resectional surgery (segmental resection, lobectomy or pneumonectomy) there is an immediate postoperative change (if adequate resection has been done) with conversion of positive to negative cultures. In pneumothorax and thoracoplasty (less so in pneumoperitoneum) the infiltration is not easily visible and the cultures are an important indication of the effectiveness of therapy and help in evaluation of the tuberculosis. With well established pneumothorax or pneumoperitoneum, or after thoracoplasty, the reappearance of positive cultures could mean the presence of reactivated tuberculosis in the operative or collapsed side or contralateral lung, or they could precede the appearance of a new lesion or indicate premature re-expansion of the collapsed lung. In resectional cases the postoperative finding of positive cultures could indicate active residual disease in the operative side or contralateral lung, or endobronchial tuberculosis or tuberculosis in the bronchial stump. In other words, if the treatment is successful, the cultures become and continue negative.

The entire question concerning cultures has been dealt with at length because they are of considerable importance in the management of tuberculosis, and to judge prognosis and therapy on the basis of concentrates alone is injudicious. Many roentgenologic changes can take place with only the cultures positive and all concentrates negative. The sensitivity of cultures is such that they are the final bacteriologic specimens to become negative and often the first to warn of active unstable tuberculosis. The changes in the tuberculous lesion occur at a gradual or rapid pace and each positive culture is not necessarily associated at the same time with alteration in the infiltration; but with the total positive reports,

resolution or progression will be evident. With the use of cultures proper determination of the patient's status is therefore possible. These bacteriologic findings must, however, be combined with clinical and roentgenologic data. With careful observation, repeated laboratory studies and serial roentgenograms, proper handling of the patient can be accomplished.

The utilization of cultures in management of tuberculosis is recommended by the National Tuberculosis Association.[16] To classify a patient as inactive requires (besides stability of the lesion and lack of cavitation) the sputum to be negative not only by concentration but also by culture or animal inoculation during a period of at least six months.

Non-tuberculous Bronchopulmonary Infections. The sputum examination is of tremendous importance in the diagnosis and treatment of the different bronchopulmonary diseases. The sputum analysis should consist of (besides determination of gross characteristics) a Gram smear, general culture and antibiotic sensitivity test. The results from this work-up are available in the usual infections within a period of twenty-four hours. With an accurate bacteriologic diagnosis and the antimicrobial agent of choice indicated, proper treatment can be initiated without delay. This plan is possible because of the availability of many antimicrobials and their known effectiveness in the various infections. If antibiotic sensitivity tests are impractical or unavailable, at least isolation of the predominant organisms in the sputum will permit appropriate treatment. Sometimes patients are treated without sputum analysis with change from one antibiotic to another until the right one or combination of drugs proves effective. A clinical trial of this kind may take time and the delay may be dangerous to the patient's ultimate recovery; also, the prolonged illness can entail economic hardships. Moreover, because of the possibility of resistance of the patient's organisms to one or more antimicrobials, cross resistance and allergic sensitivity to the drugs, serious infection with fungi or bacteria from alteration of the normal bacterial flora and gastrointestinal or other disturbances, it is essential to keep the number of drugs to a minimum and to utilize the most effective agent when treatment is initiated.

For good sputum results an adequate specimen collected properly is essential. To eliminate mouth organisms, yeasts and saprophytes, the teeth and gums should be brushed and a good throat gargle and mouth wash used (peroxide, permanganate or other antiseptic solution). The sputum container must be sterile and the patient instructed about raising fresh sputum from the chest and expectorating into the bottle. The patient can furnish a specimen of sputum raised on awakening or early in the morning (when there is usually more expectoration) or the sputum can be obtained fresh during the physical examination. In either case the sputum should be kept refrigerated until it can be examined. Stasis of unrefrigerated sputum will yield secondary organisms, putrefactive bacteria, yeasts or fungi that may contaminate and ruin the culture and antibiotic sensitivity tests. It is therefore advisable to have the bacteriologic examination done without delay. There may be no sputum available in patients too young, too sick, too old or uncooperative, or those with a dry cough. In these circumstances tracheal swabs (or having the patient cough with a sterile applicator placed above the base of the tongue in line with the droplet spray from the larynx) can be a satisfactory way to obtain enough material for smear, culture and antibiotic sensitivity tests.

Pneumonia. The sputum examination can reveal the exact etiologic cause in the various specific lobar pneumonias, namely, pneumococcic, Friedländer's (klebsiella), staphylococcic, hemolytic streptococcic and influenzal. With the proper antibiotic a specific effect is possible with full, rapid control of the infection and prevention of complications such as chronic suppuration, abscess or empyema. In most pneumonias more than one antimicrobial is usable and there may be varying sensitivity of the organisms to the different drugs; sputum culture and antibiotic sensitivity tests then provide direct answer for the most effective agent. If these tests are not possible, at least a Gram smear will indicate the organism causing the pneumonia; and appropriate therapy will thereby be achievable. The gross appearance of the sputum is not always characteristic in the different pneumonias and reliance should be placed on bacteriologic diagnosis. With resolution of the pneumonia, the sputum clears, losing its rusty appearance and purulence until all expectoration is eliminated. If there is progression of the disease or delayed resolution,

the sputum will continue or again increase in amount and may be rusty and purulent once more. In any unresolved pneumonia it is most important to search for tubercle bacilli, Friedländer's bacillus, streptococci, staphylococci, anaerobes and fungi (also tumor cells). The sputum will also change in character and increase in amount if lung abscess forms.

The sputum examination in primary atypical viral pneumonia reveals no predominating bacteria, and the organisms present are those usually found in the upper respiratory tract. The isolation of the virus from the sputum or blood stream is not an easy or practical procedure. Complement fixation or serologic procedures and cold agglutinin tests have been used in diagnosis. Secondary organisms of clinical significance can be present in the sputum and these would respond to therapy.

Sputum analysis can be of help in the diagnosis of lipoid pneumonia (following the use of iodized oil or mineral oil) by showing the fat particles or droplets. The sputum findings are important in evaluating the need of surgery as this condition often occurs in elderly patients and resembles carcinoma.

Bronchopneumonia may be primary with no predisposing cause but more often is secondary as a complication of childhood infections (measles, pertussis), chronic diseases (chronic bronchitis, bronchiectasis), epidemics (respiratory infection and influenza) or occurs terminally in debilitated or senile patients. Sputum examination can reveal many kinds of bacteria. However, one organism may predominate and sputum culture and antibiotic sensitivity tests are indicated so that proper antimicrobial therapy can be instituted.

Lung Abscess. The sputum examination is of significant importance in lung abscess. Before the lesion drains, there is little sputum; and later there is considerable expectoration of characteristically foul pus. With lung destruction the sputum shows small lung tissue fragments and elastic fibers. Sputum analysis is also valuable in differential diagnosis to rule out tuberculosis, fungus disease and neoplasms which can resemble lung abscesss.

Lung abscess can be putrid or non-putrid and due to aerobic or anaerobic bacteria. In any case, usually more than one organism is involved. The bacterial flora will depend on the etiologic factors involved in the abscess formation. In abscess due to aspiration (anesthesia, coma, postoperative (tonsils, teeth, etc.) the organisms, especially anaerobes, capable of putrid abscess formation, are those usually inhabiting the mouth, tonsils and nasal passages. These include hemolytic streptococci, spirochetes, fusiform bacilli, vibrios and gram-negative bacilli. In non-putrid aerobic infections the organisms include pneumococci, staphylococci and streptococci. In abscesses secondary to embolization the bacteria found in the sputum will depend on the source of the thrombus. The postpneumonic abscesses are more often due to specific organisms such as Friedländer's bacillus, type III pneumococcus, staphylococcus or streptococcus. Infections contiguous to the lungs (mediastinum, esophagus, subdiaphragmatic, pleural) can be responsible for abscess formation with the particular organisms involved. Lung abscess occurs in about 10 per cent of neoplasms due to bronchial obstruction and secondary infection. With trauma to the lung, infection can be brought in from the outside. In the nonspecific abscesses a multitude of organisms are involved. In these some bacteria which are ordinarily non-pathogenic, in combination or in symbiosis, become virulent.

In every lung abscess the sputum work-up should include Gram smear, aerobic and anaerobic cultures and antibiotic sensitivity test. With this information the proper therapeutic regimen can be advised.

Acute Bronchitis. The sputum at first is clear and tenacious later abundant and mucopurulent, finally mucoid and then stops entirely. Bacteriologic examination will show mixed flora although there may be predominance of a particular organism.

In acute laryngotracheobronchitis prompt treatment is necessary because of the marked toxemia, edema of the larynx and subglottic areas, and obstructive bronchial secretions. The sputum most commonly shows Staphylococcus aureus or hemolytic streptococcus, although occasionally Hemophilus influenzae is found and even viral etiology has been considered.

Chronic Bronchitis. This is rarely a primary independent infection and is usually secondary to other conditions, being associated with emphysema, neoplasm, bronchiectasis, tuberculosis, fungus disease, cardiac decompensation, etc. Chronic bronchitis is particularly common in the aged and exacerbations are

frequent during the winter months. Because the pulmonary reserve is poor and any intercurrent infection can be fatal, in some clinics antibiotic prophylaxis has been considered in the elderly to prevent the respiratory episodes. The bronchitis is hazardous in emphysema as the purulent material narrows the bronchi, and the poor tussive mechanism and lack of good bronchial drainage aggravate the diminished pulmonary function. It is imperative to control and eliminate the bronchial infection as soon as possible. The sputum examination (smear, culture and antibiotic sensitivity test) will determine the choice of the most effective antimicrobial agent. The antimicrobials are indicated even though the patient has no fever or evidence of acute illness.

The sputum in chronic bronchitis will vary. Between the intercurrent exacerbations it may be small in amount, mucoid or mucopurulent. With a new acute infection it will increase and be purulent, greenish or even foul and occasionally blood-streaked. If the bronchitis is associated with cardiac decompensation (especially mitral stenosis), the sputum may be hemorrhagic and contain heart failure cells. In putrid bronchitis the sputum will be fetid (like abscess) but microscopic examination will not show elastic fibers. Bacteriologic examination will show a mixed flora of bacteria but there is usually a preponderance of one kind of organism.

Bronchiectasis. Bronchiectasis is related etiologically to bronchial obstruction and bronchial infection. It follows pneumonia, chronic bronchitis, hilar lymph node obstruction, foreign body aspiration, atelectasis and infection with pleurisy, and is associated with other pulmonary diseases such as tuberculosis, tumor, abscess and fungus infection.

The sputum varies in amount depending on the severity of the bronchiectasis, the presence of intercurrent infection and weather conditions. Cough and expectoration are increased during acute infections, cold damp weather and by postural drainage.

The sputum will vary in type from mucopurulent to thick purulent and from light yellow to heavy greenish yellow. It characteristically forms three layers on standing (bottom layer of pus and cellular debris, middle layer of mucus and pus, and a top frothy mucoid layer). This layering also occurs in lung abscess or gangrene. The sputum will often contain blood in varying amounts. The odor is musty or fetid depending on the type of infection.

Microscopic examination of the sputum will reveal a mixed flora of gram-positive and gram-negative organisms. Sputum analysis is always advisable in bronchiectasis to rule out the presence of tubercle bacilli. Although there is a mixed flora, the predominant specific pathogens will be evident and the antibiotic sensitivity tests will indicate the antimicrobial agent to be used. Such medical treatment is employed palliatively in patients ineligible for surgery or for preoperative preparation. The definitive treatment in bronchiectasis is surgical removal of the involved area. Specific antimicrobial agents will usually result in definite clinical improvement. This amelioration may be only temporary. Either recurrent or new infection takes place or the bacterial flora may change with other predominant strains of organisms apparent. The sputum tests should therefore be repeated to guide proper therapy.

Allergic Bronchial Disease. The most important sputum finding in allergic bronchial disease is the presence of eosinophils. The number of eosinophils may vary and more than one sputum should be examined.

In uncomplicated asthma there is usually characteristic sputum—thick, tenacious, greyish white mucoid material. Bronchial infection is a common complication of asthma and the allergy may be associated with sensitivity to the bronchitis—"infective asthma." If there is much secondary infection, there will be considerable sputum of a mucopurulent or purulent character.

Although the sputum will contain a mixed flora, there is usually a predominant organism. It is very important to do sputum studies with smear, culture and antibiotic sensitivity tests so that the appropriate antimicrobial can be used from the beginning. In this manner the bronchial infection can be cleared. Because of the hazard of drug sensitivity in these allergic individuals a clinical trial with different antimicrobial agents is not desirable.

Influenza. This is of two types, the mild winter grippe epidemics and the severe pandemic infections. In mild influenza the sputum has no unusual characteristics. In the severe form there is an overwhelming virulent involvement of the lungs with a viral toxic agent or infection due to different predominant organisms, particularly the Streptococcus he-

molyticus, pneumococcus, influenzal bacillus or Staph. aureus. These pneumonias are characterized by considerable hemorrhagic edema of the lungs or marked bacterial invasion and suppuration. The sputum is bloody or purulent, with enormous numbers of the predominant organism.

Lung Cyst. Pulmonary cysts which are ordinarily air-bearing or partially filled with clear secretions not infrequently become infected. They then contain purulent material and an acute illness results which resembles lung abscess. The sputum examination is important for bacteriologic diagnosis and the appropriate antimicrobial agent can be used.

Fungus Infection. There are a number of fungi which can be pathogenic and are capable of causing pulmonary disease. Included in the list are the following: actinomycosis, North American blastomycosis, coccidioidomycosis, geotrichosis, cryptococcosis, moniliasis, histoplasmosis and aspergillosis. The presence of the fungus in the sputum does not always mean it is pathogenic. Some fungi are saprophytic, common inhabitants of the respiratory tract, or secondary invaders which accompany other diseases such as tuberculosis, bronchiectasis and lung abscess. Other fungi, like monilia, are more prevalent in sputum after much use of antibiotics.

To make the diagnosis it is important to collect fresh sputum after preliminary preparation (cleansing teeth and gums and throat gargle). The fungi can be found by direct examination, culture or animal inoculation. Direct examination includes a fresh slide or cover glass preparation of sputum or a Gram smear. To be significant the fungi must be found persistently and abundantly in sputum (with other etiologic agents excluded). Culture methods are of great value in the isolation and identification of fungi. Specific or special media are employed for this purpose. Animal inoculation determines the pathogenicity of the fungi. For this either sputum or a saline suspension of the pure culture is used and results are usually rapidly available.

If the sputum is inadequate, gastric contents can be aspirated for direct examination and culture. Examination of the sputum is an important method of diagnosis in fungus disease. However, in addition there are usable skin tests, and complement fixation, precipitin and agglutinin tests are available.

The foregoing laboratory findings must be correlated with the special clinical and x-ray features of the illness. Fungus disease can resemble tuberculosis, lung abscess and other bacterial infections. In any obscure case of chronic lung lesion or chronic pulmonary suppuration, particularly with sputum negative for tubercle bacilli, a fungus condition must be considered.

Neoplasm. It is not within the scope of this paper to discuss the tremendous importance of cytologic studies of sputum or bronchoscopic aspirations in the diagnosis of neoplasm. Suffice it to say that in competent laboratory hands studies for tumor cells will be positive in a majority of cases of neoplasm. From a bacteriologic point of view the sputum findings will vary with the degree of bronchial infection and bronchial obstruction. Thus there can be little or abundant sputum, with gradations from mucoid, mucopurulent, purulent to even foul expectoration. At some time in almost half of the cases there will be blood in the sputum. With considerable bronchial obstruction there is severe secondary infection and chronic pulmonary suppuration, and the sputum findings resemble that found in lung abscess and bronchiectasis. On occasion with necrosis of the neoplasm, small tumor particles may be found in the sputum. The sputum examination can also provide information about the effective antimicrobial agents that could help the infection. Such therapy would be used on a preoperative basis or for palliation in individuals ineligible for surgery.

Infarction. In typical infarction in a patient with no previous lung infection and a nonseptic embolus, the sputum will be composed mainly of mucoid bloody material and few bacteria. If there is pre-existing pulmonary infection or the embolus is septic or breakdown of the infarcted area is associated with secondary infection, there will be much sputum composed of blood mixed with purulent material and many bacteria. Control of the infection is urgent in these usually seriously ill patients. Sputum analysis will indicate the appropriate antimicrobial agent.

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Diagnosis of Lipoid Pneumonia

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LAUGHLIN[1] in 1925 reported for the first time the occurrence of lipoid pneumonia in four children who had been treated with menthol and albolene (mineral oil) for various nose and throat infections. Autopsies performed in these cases revealed a bronchopneumonic process characterized by the presence of large phagocytes containing fat droplets which readily stained with Sudan III. He succeeded in producing comparable bronchopneumonic lesions in the rabbit following the intranasal instillation of mineral oil. Although liquid petrolatum causes the most pronounced and irreversible pulmonary lesions in man, other substances such as animal and vegetable oils have also been known to produce "proliferative pneumonitis" following intratracheal instillation in animals as shown by Guiesse-Pellissier[2] in 1920 and Corper and Freed[3] in 1922.

The various reactions to different oils such as animal or vegetable oil as well as liquid petrolatum were studied experimentally by Pinkerton in 1927 and 1928.[4,5] He demonstrated that neutral vegetable oils produced little damage with the exception of chaulmoogra oil which caused necrotizing pulmonary lesions, while some animal oils as well as mineral oil led to a more pronounced tissue reaction with proliferation of multinucleated giant cells and macrophages. The picture was similar to that in human pathology. With the attention thus focused on this condition, lipoid pneumonia, also called oil aspiration pneumonia, became widely recognized and many excellent accounts with detailed description of the clinical and pathologic manifestations were recorded in the following twenty-five years.[6–23]

Whereas lipoid pneumonia was first thought to occur only in physically handicapped infants or in chronically debilitated adults afflicted with neurologic disorders as paralysis agitans, hemiplegia, pseudobulbar palsy or deformities interfering with normal swallowing such as cleft palate or harelip, it has also been observed in apparently healthy individuals.[20,23–29] It seems to be fairly well established at the present time that the use of mineral oil as a throat lubricant or as a vehicle for nose drops as well as a laxative can cause chronic pulmonary lesions identical to those produced experimentally in animals.

The great variation in the clinical picture and the frequently atypical and inconclusive roentgenographic findings make the diagnosis of lipoid pneumonia a difficult task, particularly in the absence of a definite history of intake of mineral oil. Moreover, many patients afflicted with this condition are clinically asymptomatic.[22,30] Oil aspiration pneumonia may be confused with other pulmonary diseases such as low grade infections, tuberculosis, fungus disease, sarcoidosis or neoplasms, both benign or malignant. While lipoid pneumonia may have been previously of interest to the internist, pediatrician or pathologist only, it has gained considerable differential diagnostic significance with the recent progress achieved by thoracic surgery. The recognition of lipoid pneumonia appears of particular importance in those patients in whom a diagnosis of bronchogenic carcinoma is entertained because needless surgical intervention may be avoided whenever the correct diagnosis can be established clinically.

It has been shown by us[31] that the diagnosis of lipoid pneumonia can be corroborated with a considerable degree of accuracy by correlating the roentgenographic findings with cytologic studies of the sputum[32] as well as of material aspirated from the lungs.[33,34]

CYTOLOGIC STUDIES

Sputum. A twenty-four-hour collection of sputum is obtained daily for three to five consecutive days from patients whose history, physical examination and roentgenographic

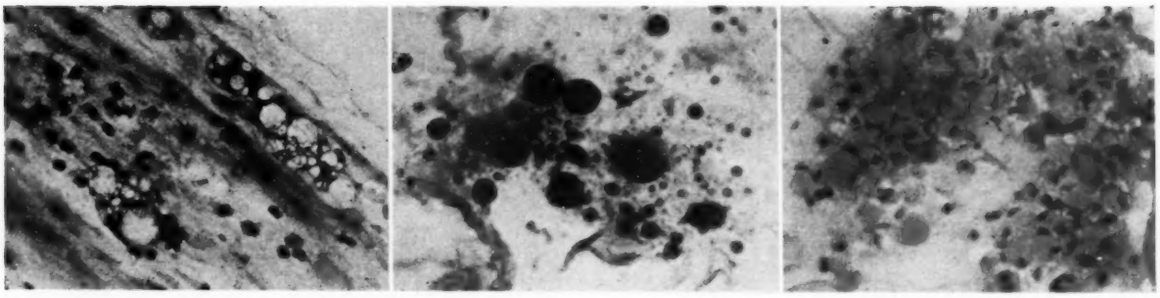

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FIG. 1. Lipophages in sputum; the vacuoles may be stained positive with Sudan IV. Wright stain, × 500.

FIG. 2. Extracellular fat-staining material in sputum. Sudan IV stain, × 350.

FIG. 3. Aspiration from the lung; clusters of lipophages. Sudan IV stain, × 400.

findings are suggestive of lipoid pneumonia. The patient is placed on a strict fat-free diet beginning four days prior to as well as throughout the period of sputum collection. A drop of sputum is deposited on each of four glass slides with a platinum loop, and a drop of saline is added to establish a thin spread. If the sputum is thin and watery, the specimen is centrifuged for five minutes; and the sediment is then spread on a glass slide in a similar manner. The slides are dried in the incubator. Two of the slides are stained with Sudan IV, and two with Wright's stain as modified by Lillie.[32] The sputum is considered positive for lipoid pneumonia when the Wright stain shows the characteristic macrophages containing clusters of vacuoles (Fig. 1) and also if these vacuoles stain orange-brown in Sudan IV or if abundant extracellular fat-staining material is present. (Fig. 2.)

Material Aspirated from the Lung. The patients are prepared by the administration of 100 to 150 mg. of demerol,® according to weight and age, about forty-five minutes prior to aspiration. Younger and physically able individuals receive an additional 0.1 gm. of seconal® about one hour prior to the injection of demerol. After local anesthesia of the site of aspiration, carefully selected with the aid of roentgenograms of the chest, a 19 gauge spinal needle with the stylet *in situ* is introduced to a depth of about 2½ inches within the lung tissue proper. After removal of the stylet a 20 ml. syringe is attached to the needle, which under forceful aspiration is slowly withdrawn. If at any point frank blood appears in the syringe, suction is stopped at once and the withdrawal is completed. A successful aspiration yields one or perhaps two blood-tinged droplets of fluid. These are ejected through the needle onto five slides where they are spread thinly. The air-dried smears are fixed in 10 per cent solution of formalin for three hours and then stained with Sudan IV and Wright's stain, similar to the procedure employed for sputum.

The aspirated material is considered positive when the characteristic lipophages, single or arranged in clusters and frequently transformed into giant cells, are observed. (Fig. 3.)

ROENTGENOGRAPHIC OBSERVATIONS

Roentgenographically, two main types of lipoid pneumonia can be distinguished: (1) a circumscribed involvement within a lobe which can easily be mistaken for a tumor (Fig. 4), and (2) a diffuse type which usually affects several lobes and is more commonly encountered. During the acute phase lipoid pneumonia gives rise to soft densities within one or several lobes of the lungs which cannot be differentiated from any other form of pneumonitis. Oil aspiration pneumonia has a predilection for the right middle and right lower lobes. The upper lobes are primarily affected in bed-ridden patients or infants. In the presence of upper lobe involvement differentiation from pulmonary tuberculosis may be difficult at times. Since lipoid pneumonia frequently undergoes fibrosis, it can cause a contraction of the involved area. The surrounding lung tissue then appears emphysematous. This fibrosis and contraction give rise to the characteristic "ground glass" appearance. (Fig. 5.) This is the best known feature of lipoid pneumonia and represents a late phase of the disease. Calcification and hilar lymphadenopathy are never observed roentgenologically. If bronchographic studies are carried out, it

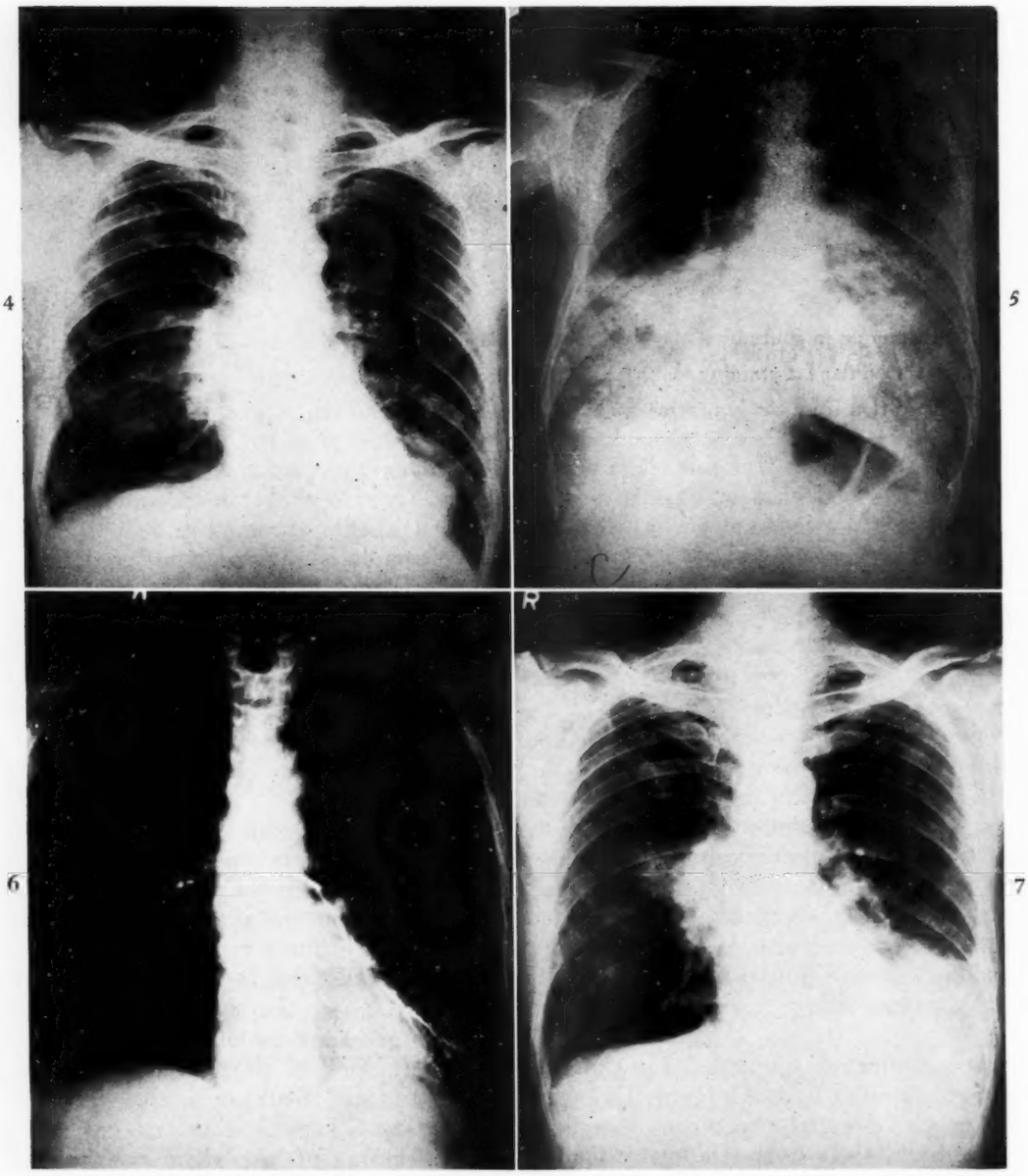

FIG. 4. Circumscribed tumor-like mass in the left lung. There is enlargement of the right hilar shadow due to involvement of the apex of the right lower lobe, not to be mistaken for hilar adenopathy.

FIG. 5. Massive involvement of both lower lobes. "Ground glass" appearance as a result of contraction of the lesion and subsequent fibrosis. No calcification seen.

FIG. 6. Lipoidol studies showing blockage of the terminal branches without filling of the alveoli (so-called "dead tree" effect).

FIG. 7. Same patient as in Fig. 4 two years later. There is some progression of the disease on the left side with lobar involvement instead of the original tumor-like mass. There is also further progression of the involvement within the apical portion of the right lower lobe.

can be noted that the bronchi skirt the mass and the terminal bronchioles are occluded and do not enter the lesion. (Fig. 6.) There is no evidence of bronchiectasis or of progression to lung abscess. It may be difficult at times to differentiate the circumscribed lesions. Contralateral involvement has invariably been demonstrated in all such instances when laminagraphic studies were done. The contralateral involvement (Fig. 7) may consist only of

small patchy infiltrations, but in conjunction with the mass lesion such a finding is helpful in establishing the diagnosis. In the presence of a clinically suspected diagnosis of lipoid pneumonia a routine postero-anterior x-ray of the chest may be inadequate. In such instances oblique and lateral views will help to uncover lesions frequently hidden by the cardiac shadow.

COMMENTS

In a previous study carried out on chronically ill patients the authors[31] were able to establish the diagnosis of lipoid pneumonia by a combined radiologic and cytologic approach. Most of these patients gave long histories of mineral oil intake. The clinical findings were not particularly characteristic, but occasionally included such symptoms as productive cough, dyspnea, febrile exacerbations and chest findings associated with pulmonary consolidation. In many instances, however, the patients were asymptomatic and the lesions were discovered by routine roentgenologic studies of the chest, at times diagnosed as bronchogenic carcinoma, particularly when circumscribed in appearance. This differential diagnosis may be particularly tempting when a mass lesion is associated with hemoptysis. This symptom has been observed, though rarely in lipoid pneumonia.[35,36] In such circumstances several writers have advocated exploratory thoracotomy with fresh frozen sections as a guide for the surgeon.[37,38] The authors, however, believe that careful combined radiologic and cytologic evaluation may help in many instances to prevent unnecessary surgical intervention.

Earlier writers have suggested that intra- or extracellular oil globules may be used as an aid in the diagnosis of lipoid pneumonia.[29,39–46] More recently, Schneider[21] demonstrated the presence of oil in aggregates of three successive morning sputums by covering a spread of the latter on a glass slide with cigarette or lens paper or by staining these oil droplets with scarlet red. Nuessle,[50] on the other hand, reported that free fat globules may occur in normal individuals without any evidence of pulmonary disease. In these instances he even noted occasional macrophages containing Sudan-staining material. While the authors concur with the observation that small amounts of sudanophilic material may be found in normal sputum, no lipophages were encountered in our control subjects. Furthermore, the diagnosis of lipoid pneumonia was entertained only in patients with abundant free sudanophilic material as well as with a distinct number of characteristic lipophages in the sputum. These cytologic prerequisites were corroborated with the positive findings in the material aspirated from the lungs.

It was observed previously by us[31,32] that in several patients serial daily sputum examinations were required before fat-staining material was found even in patients whose chest roentgenograms were consistent with the diagnosis of lipoid pneumonia. Whenever possible the direct aspiration from the lung was performed under the guidance of x-ray films. In those patients, however, who were negative radiologically but whose history and clinical symptoms were suggestive of lipoid pneumonia, a point in the ninth intercostal space posteriorly and 3 inches to the right of the spinal column was selected for aspiration since in our experience the lesions were most frequently found in this location. In a few instances repeated aspirations had to be performed before evidence of lipoid pneumonia was obtained.

The only untoward effect encountered with this procedure in a few patients only was an asymptomatic short-lasting pneumothorax as well as aspiration of blood which occurred in four of over eighty subjects. The bleeding was never found to cause major complications except for the fact that the sputum remained blood-tinged for about three or four days.

Since Pinkerton's[4,5] classic studies of the reactions of oils and fats on pulmonary tissue in 1927 and 1928, little has been added to our knowledge on this subject. Of the various agents producing the picture of oil aspiration pneumonia which include cod liver oil, milk fat, iodized oil or mineral oil, the latter is the most common cause of lipoid pneumonia since it is widely used as a laxative as well as a vehicle for nose drops, throat lubricants or various oil-containing medications. Mineral oil, a hydrocarbon and not a fatty substance, is capable of entering the bronchial tree without exciting the reflex inhibition. It therefore flows readily from the pharynx into the tracheobronchial tree. This has been shown in animal experiments by demonstrating that liquid petrolatum fails to produce a cough reflex, and therefore does not stimulate reflex closure

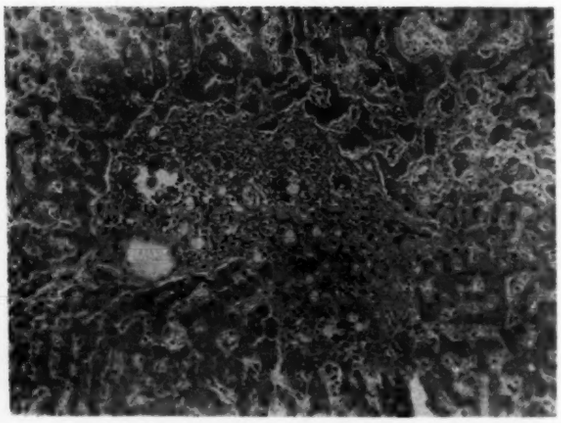

FIG. 8. Granuloma-like lesion of the liver containing lipophages. The vacuoles may be stained with Sudan IV. Hematoxylin and eosin stain, × 150.

of the glottis.[51,52] Many of the commonly used nose drops impair the ciliary activity and even destroy the respiratory epithelium.[53,54] In addition, it was demonstrated experimentally that mineral oil hinders the ciliary movement mechanically by slowing or stopping the flow of mucus covering the cilia, thus considerably impairing their normal activity.[55] Cannon and Walsh[56] studied the development of "oil granuloma" experimentally by injecting purified mineral oil intratracheally into rabbits. They observed an initial pulmonary edema and postulated that the oil caused injury to the pulmonary capillaries which led to an increase in capillary permeability and seepage of albumin into the alveoli. A reticulum of collagenous fibers developed between the macrophages and within the alveoli. The oil became fixed in fibrous tissue, thus obliterating many of the air spaces. Within the fibrous tissue, areas of necrosis surrounded by giant cells and epithelioid cells were found giving the microscopic picture of a granuloma.

In man the tissue reaction in the lung following ingestion of liquid petrolatum is similar to that of the experimental animal. Fine droplets of mineral oil are phagocytized by large macrophages, called "foam cells" or "lipophages," which accumulate in large numbers at the site filling the air spaces. Occasionally a mild inflammatory reaction develops temporarily in the alveoli, which may involve also the bronchioli and peribronchial tissue. Necrosis is hardly ever observed in the lung. However, a reticulum of collagenous fibers is laid down between the foam cells and the phagocytized material becomes fixed by the immobilized lipophages and the connective tissue which penetrates between the cells and also surrounds them. Since mineral oil is insoluble, it acts as a foreign body in the tissue and stimulates the proliferation of giant cells. In older lesions the alveolar walls are thickened by fibrous tissue and the alveoli are lined by cuboidal cells. Such lesions are practically permanent, constituting tumor-like masses of granulomatous tissue and are called "paraffinoma." It is this lesion which roentgenologically resembles a neoplasm.

Our previous studies suggest that macrophages frequently disintegrate, thus setting free the intracellular fat-staining material. The oil may be expectorated or it may be carried to the regional hilar lymph glands. There are several cases on record in which deposits of lipoid material or macrophages have been found in various viscera such as the liver, spleen, kidneys or adrenals, usually forming granuloma-like lesions.[57,58] In our own autopsy material such lesions were also observed in three instances in the liver (Fig. 8) and spleen, and are believed to be embolic phenomena secondary to paraffinoma of the lung. In many instances the lipoid material liberated from the disintegrated lipophages may be reaspirated from the upper bronchial tree and returned to the alveoli, thus producing a vicious cycle by stimulating proliferation of macrophages and eventually causing fibrosis. This may account in part for the chronicity of the process even after oral or nasal intake of lipoid material has long been discontinued. Moreover, the lack of saponification of mineral oil makes its assimilation and absorption impossible. It is primarily in the chonic lesions that the sputums are negative for fat-staining material, since the aspirated substance becomes encapsulated by connective tissue and since the alveolar ducts or respiratory bronchioles become plugged by inspissated material which had accumulated in the areas of consolidation. Hence it is believed that in these cases the transthoracic aspiration of material from the lungs offers a superior means to obtain the diagnostic lipophages.

The question whether liquid petrolatum has carcinogenic activity has been repeatedly brought forth through the years. There are some experimental reports as well as occasional cases recorded in the literature. For instance Shimkin[59,60] and Twort and Lyth[61] succeeded

in the production of lung tumors in mice by intratracheal instillations of mineral oil. These substances, however, were rather aromatic hydrocarbon-like methylcholanthrene and benzopyrene and not saturated alipathic hydrocarbons, commonly called mineral oil. Moreover, most of these tumors originated from the alveolar epithelium and not in the bronchial tree. There are several cases reported in which bronchogenic carcinoma was associated with a history of mineral oil intake for years, suggesting a possible carcinogenic effect of this substance.[49,62] However, the majority of observers agree that there is not sufficient clinical or pathologic evidence so far to substantiate any carcinogenic properties of liquid petrolatum. In our material of more than eighty patients with lipoid pneumonia, many of whom were under constant medical supervision for as long as twenty years and most of whom were in the cancer age group, there has not been a single instance of complicating bronchogenic carcinoma.

Although the differential diagnosis of lipoid pneumonia appears to be of paramount importance in those patients in whom the roentgenologic findings simulate a pulmonary malignancy, the diagnosis of lipoid pneumonia may also be of considerable value in those conditions, which are mistaken for other low grade pulmonary infections, bronchiectasis, mycoses or sarcoidosis since the correct identification of these diseases may be helpful as to therapeutic procedures contemplated. Furthermore, the spread of the lesion can be prevented by discontinuing further intake of mineral oil or other oil-containing medications when the diagnosis is established early.

SUMMARY

1. Lipoid pneumonia occurs not only in chronically debilitated adults or in physically handicapped children, but also has been observed in apparently healthy individuals. Mineral oil is the most common cause of this condition since it is widely used as a mild laxative as well as a vehicle for oily nose drops, thorat lubricants or various oil-containing medications.

2. The differential diagnosis of lipoid pneumonia frequently causes considerable difficulty since this condition may be confused with other pulmonary diseases such as low grade infections, tuberculosis, fungus disease, sarcoidosis or benign and malignant neoplasms.

3. The recognition of lipoid pneumonia is of particular importance in those patients in whom a diagnosis of bronchogenic carcinoma is entertained because needless surgical intervention may be avoided.

4. The clinical findings are not characteristic, and include productive cough, dyspnea, febrile exacerbations and chest findings associated with pulmonary consolidation. In many instances the patients are asymptomatic.

5. The diagnosis of lipoid pneumonia can be established clinically with a considerable degree of accuracy by correlating the roentgenographic findings with cytologic studies of the sputum as well as of material aspirated transthoracically from the lung.

6. The positive sputum contains lipophages and abundant amounts of free sudanophilic material, while the material aspirated from the lung is considered positive when the characteristic lipophages, single or arranged in clusters and frequently transformed into giant cells, are found.

7. The roentgenographic features indicative of lipoid pneumonia are discussed.

8. The mechanism of the progressive nature of the disease after discontinuance of the inciting liquid petrolatum is suggested as being due to reaspiration of disintegrated lipophages.

9. Early clinical recognition of lipoid pneumonia may prevent extensive spread of the pulmonary involvement by discontinuing the intake of mineral oil or other oil-containing medications.

Acknowledgment: The authors wish to express their appreciation to Mr. Herbert A. Fischler for the illustrations included in this study.

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Lung Biopsy for the Diagnosis of Disseminated Pulmonary Disease

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THE term disseminated pulmonary disease is applied to cases in which chest roentgenographic examination shows lesions scattered throughout both lungs. Some patients presenting these findings are discovered in surveys and are asymptomatic, while others seek medical advice with symptoms of pulmonary disease. Chest roentgenograms are not diagnostic. Disseminated pulmonary disease, regardless of etiology, may have a similar distribution and configuration of the x-ray lesions. Bronchoscopic examinations of these patients with cytologic and bacteriologic studies of aspirated secretions may provide a diagnosis of carcinoma, tuberculosis or some bacterial or fungous infection. Skin tests may in some cases suggest the presence of histoplasmosis, coccidioidomycosis, tularemia, blastomycosis or toxoplasmosis but even when positive these may be unrelated to the lesions under investigation.

In the majority of patients disseminated pulmonary disease remains undiagnosed following the usual clinical studies. These patients are subjected to interval chest roentgenograms. Several diagnoses are suggested and a period of "watchful waiting" ensues. No one can deny that adequate treatment of a patient requires an accurate diagnosis; however, this principle is infrequently applied in these patients. They receive non-specific therapy or none at all. The patient shares the physician's uncertainty about his future. He is not told when he can return to work and no positive report can be given, if necessary, for compensation purposes.

Physicians readily accept the urgency of performing an exploratory thoracotomy on patients with unilateral lesions suspected of being neoplastic. It is not widely realized, however, that biopsy is equally important in patients with undiagnosed disseminated pulmonary disease.

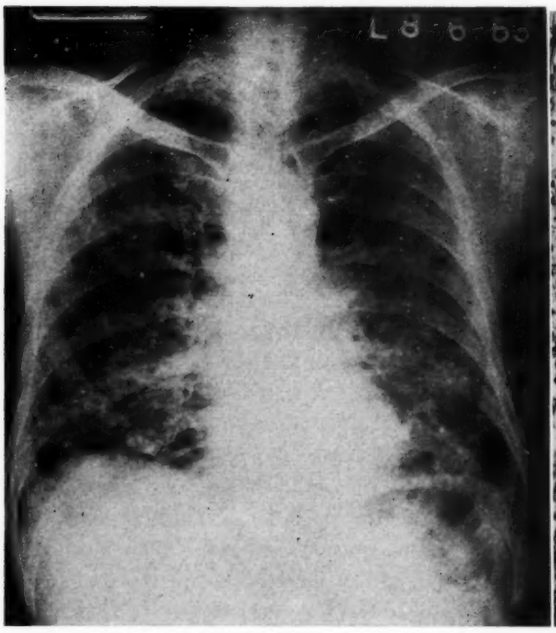
A variety of biopsy technics have been used. Liver biopsy, peripheral node biopsy or bone marrow biopsy may provide a histologic diagnosis if the disseminated pulmonary disease is associated with a systemic condition. Biopsy of scalene lymph nodes has been suggested by Daniels[1] for the diagnosis of intrathoracic disease. These nodes are part of the chain of deep mediastinal nodes and likely to be involved in the same pathologic process. If the disseminated pulmonary disease cannot be diagnosed by the usual clinical studies and the patient does not present associated involvement of other organs, a lung biopsy should be performed.

Needle biopsy of the lung, either by aspiration or with a Vim-Silverman needle, is unsatisfactory in this type of pulmonary disease. It is a blind procedure which may be complicated by hemorrhage or pneumothorax and it does not provide sufficient tissue for histologic and bacteriologic study, or chemical analysis. Direct biopsy of the lung through the usual open thoracotomy readily provides adequate tissue for examination but it is too drastic a procedure for many patients with pulmonary insufficiency. The method of Klassen[2] for pulmonary biopsy gives equally good results with little or no morbidity and very little discomfort. In a recent report[3] this technic was used in eighty-seven cases, with no mortality or complications. The Klassen procedure is performed under local anesthesia through an intercostal incision. The wound is closed without the usual uncomfortable drainage tube and patients are out of bed on the day of operation and leave the hospital on the third postoperative day.

The following cases illustrate the use of pulmonary biopsy in the diagnosis of disseminated pulmonary disease.

CASE REPORTS

CASE 1. T. P., a fifty-three year old white male, was admitted to the Philadelphia Veterans Administration Hospital in July, 1953. He gave a history of having had a "cigarette cough" for many years and a productive cough, progressive dyspnea and weight loss



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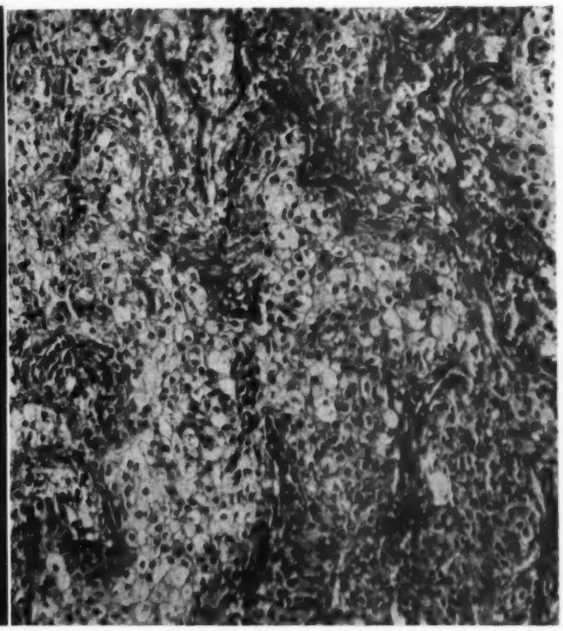

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FIG. 1. Case 1. Posterior-anterior roentgenogram of the chest showing enlarged hilar shadows and disseminated infiltrations and fibrosis throughout both lungs.

FIG. 2. Case 1. Photomicrograph of lung section showing a great accumulation of lipophages. The alveoli septa are still visible although compressed by the large numbers of lipid-laden cells within the alveolar spaces. Diagnosis was lipoid pneumonitis; × 200.

during the past two years. Walking 10 or 15 feet brought on a state of collapse. Physical examination showed advanced pulmonary osteoarthropathy and an emphysematous chest with crepitant rales throughout both lungs. Chest roentgenogram (Fig. 1) showed disseminated lesions throughout both lungs. Laboratory studies, including hemograms, urinalysis, serology, blood chemistries and liver function tests were normal. Sputum studies were non-specific. The tuberculin test was positive. The patient improved after treatment with antibiotics, bronchial dilating drugs and intermittent positive pressure breathing therapy. A lung biopsy was performed. Microscopic examination (Fig. 2) revealed a diagnosis of lipoid pneumonitis.

Comment. This patient had not been exposed to any exogenous sources of oil such as oily nose drops or mineral oil laxatives. The tissue changes could be the result of non-specific infections with secondary tissue destruction with histiocytes taking up cholesterol and lipid substances. This case probably represents a form of endogenous lipoid pneumonitis. Although an exact etiologic diagnosis could not be established, we felt justified in giving the patient cortisone which brought about further improvement in his condition.

CASE II. J. C., a twenty-nine year old white male, gave a history of working in a beryllium steel plant in 1942 for only four weeks. In 1945 while in the Army he complained of dyspnea and cough on exertion. These symptoms became progressively worse and he was hospitalized in 1952. A diagnosis of either sarcoidosis or beryllium granulomatosis was considered at that time. Cortisone was administered and temporary improvement was noted. He was admitted to the Philadelphia Veterans Administration Hospital in November, 1953, complaining of severe dyspnea on exertion. The tuberculin test was negative. Laboratory studies, including liver function tests, were normal. His vital capacity was 2,130 cc. in three seconds, and his maximal breathing capacity was 70 L./min., 63 per cent of his expected normal. Chest roentgenogram (Fig. 3) revealed disseminated lesions throughout both lungs. This patient was well informed concerning his condition and had filed a pension claim insisting that he had sarcoidosis which had developed in the Army. A lung biopsy was performed. Microscopic section (Fig. 4) of lung revealed focal granulomas and fibrosis. These findings were consistent with a diagnosis of berylliosis or sarcoidosis. Some of this tissue

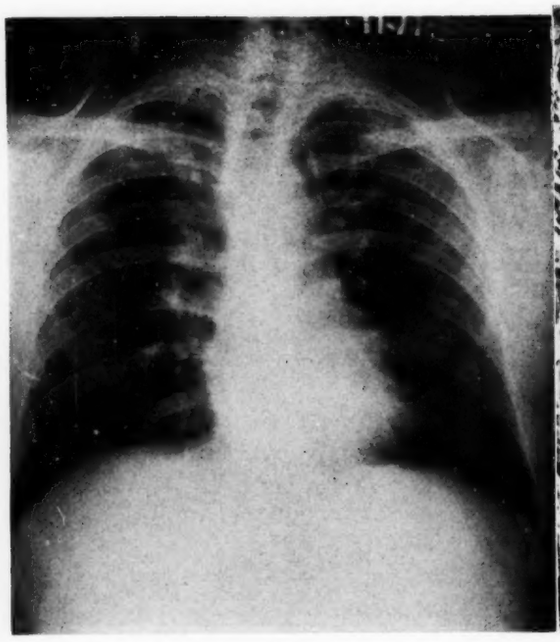

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FIG. 3. Case II. Posterior-anterior roentgenogram of the chest showing fine nodular densities scattered throughout both lungs.

FIG. 4. Case II. Photomicrograph of lung section reveals two granulomas and fibrosis. The granulomas are composed of epitheloid cells and giant cells. Diagnosis was focal granulomas and fibrosis; × 200.

was sent to Dr. Harriet Hardy of Boston for beryllium analysis. It showed 2.22 μg of beryllium per 100 gm. of tissue. This finding made a specific diagnosis in this case of delayed beryllium granulomatosis.

Comment. The diagnosis of berylliosis provided a sounder basis for cortisone therapy and showed that the patient's disability resulted from an industrial hazard and was not incurred in military service.

CASE III. E. E., a thirty-six year old white male, was in good health until 1937 when acute rheumatic fever developed while he was in military service. He states that after four months of bedrest he recovered and was returned to duty. In 1942 he noticed shortness of breath while on marches but he did not report to sick call, and subsequently went overseas. In 1943, following hospitalization for injuries received in a motorcycle accident, he was told that he had heart disease and was reassigned to light duties. The shortness of breath became progressively worse and he began to suffer from excessive fatigue after exertion. He was discharged from the Army but was able to perform light work until December, 1952, when malaise, fatigue, weakness and fever developed. He was treated in a hospital for subacute bacterial endocarditis and in August, 1953, returned to work with instructions to take digitalis. A few months later fatigue, malaise and progressive shortness of breath again developed. In February, 1954, he became febrile and was admitted to the Philadelphia Veterans Administration Hospital.

Physical examination showed a well developed white male in no apparent discomfort. Scattered crepitant rales were heard at the bases of both lungs. On percussion the left border of the heart was just outside the midclavicular line. A grade 3 systolic murmur was heard in the third left interspace. There was a split aortic second sound. No diastolic murmur was heard. An electrocardiogram showed auricular fibrillation with a well controlled ventricular rate of 70 per minute and right axis deviation. Phonocardiograms recorded a faint systolic murmur at all valve areas. No diastolic murmur was recorded. Roentgenogram of the chest (Fig. 5) revealed disseminated lesions scattered throughout both lung fields. A heart study showed left auricular, right ventricular and pulmonary artery segment enlargement.

His venous pressure was 45 mm. of water. The arm-to-tongue circulation time was twenty-two seconds. The white blood count

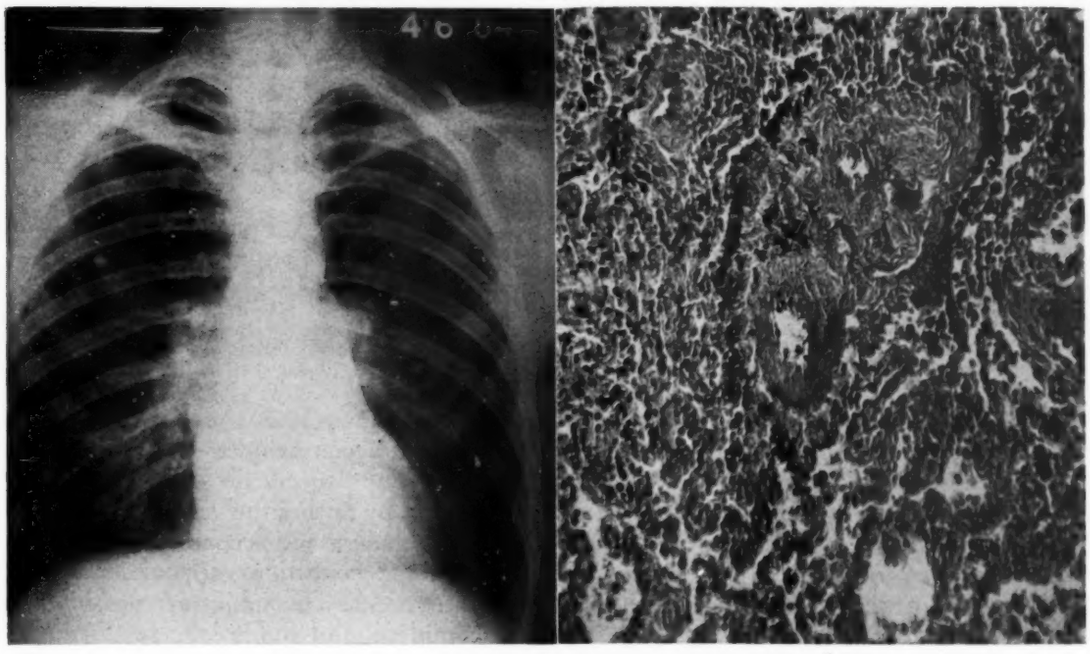

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FIG. 5. Case III. Posterior-anterior roentgenogram of chest showing fine nodular densities scattered throughout both lungs and enlarged pulmonary artery segment.

FIG. 6. Case III. Photomicrograph showing vascular sclerosis (pigment-bearing macrophages within alveolar spaces). Special stains demonstrated pigment to be iron; × 110.

was 11,000/cu. mm. with 70 per cent neutrophils; sedimentation rate was 41 mm. per hour. Antistreptolysin titer was 48 and antihyaluronidase titer, 512. Other laboratory studies were not significant.

The patient improved on bedrest and his temperature, white blood count and sedimentation rate returned to normal. It was believed that the patient had rheumatic heart disease, probably with recent activity. He also had some disseminated pulmonary disease. The possibility of hemosiderosis was questioned because of the lack of severity of the heart disease and absence of the diastolic murmur of mitral stenosis. It was thought that this patient might have some primary pulmonary disease contributing to his symptoms. Sputum studies were negative for acid-fast bacilli. Skin tests for tuberculin, coccidioidin and histoplasmin were negative.

A lung biopsy was performed May, 1954. Microscopic section of lung (Fig. 6) showed congestion with iron-laden macrophages.

Comment. The specific diagnosis obtained by biopsy permitted us to consider this patient for mitral commissurotomy. The clinical studies alone did not rule out the possibility of some primary pulmonary disease that would have been a contraindication to cardiac surgery.

SUMMARY

1. The importance of performing a lung biopsy in the presence of undiagnosed disseminated pulmonary disease is discussed.

2. Cases are presented to demonstrate the usefulness of this procedure.

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Problems in the Roentgen Differential Diagnosis of Bronchopulmonary Diseases

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ROENTGEN examination of the chest has given the clinician a method of investigation which in many instances is superior to the clinical technics of physical diagnosis because it permits a visualization of changes due to pathologic processes. This method unfortunately is subject to the pitfalls and errors common to all fields of medicine. Not only are there wide variations in the boundaries of the "normal" roentgen appearances, but also the so-called characteristic pathologic roentgen signs show a lack of specificity and are rarely pathognomonic. There are x-ray signs, of course, that are fairly typical of certain lesions so that a "working diagnosis" can often be made which is satisfactory for the initial management of the patient. A description of a roentgen finding is, however, no more a diagnosis of chest disease than is a description of a physical finding.

The language of radiology is not ideally suited for describing the roentgen findings. It includes a conglomeration of terms borrowed from other branches of medicine such as anatomy, pathology and clinical medicine. Usually the terms describe the roentgen appearance with the implication of its normal or pathologic anatomy, e.g., peribronchial infiltration, segmental consolidation; occasionally the terms make no pretence at disguise but bluntly stab at a definitive diagnosis, e.g., tuberculous cavity, bronchogenic carcinoma. What is even more disturbing is the misunderstanding resulting from the differing connotations often attributed to the same or similar terms.

This article will point out some of the problems that concern the description, evaluation and differential diagnosis of the roentgen findings. The accompanying tables will demonstrate the non-specificity of the roentgen findings; first, by noting the variety of lesions listed under each sign and second, by observing how often these conditions appear under several different signs. The tables are not intended to be complete, and the lesions are listed in convenient groups for purposes of discussion and not necessarily in order of importance. The composite schematic drawings are intended not only to illustrate the various roentgen signs but also to indicate the similarity of the roentgen appearances of many unrelated diseases.

PROBLEMS INHERENT IN THE ROENTGEN METHOD OF STUDY OF THE LUNGS

The relative absorption of x-rays in the range of diagnostic roentgenology is in the approximate ratio of 1,000:1 for equal thicknesses of water and air. All of the tissue components of the chest with the exception of bone have approximately the same specific gravity as water. It is obvious that the lung fields are exceptionably well suited for the demonstration on the roentgenogram of the relatively radiopaque tissues and the markedly contrasting radiolucent air. Unfortunately this advantage is offset by the nature of the conventional roentgenogram, namely, the projection on a two-dimensional surface or plane of a three-dimensional structure. (Fig. 1.) This of necessity results in a superimposition or summation of shadows which no alteration of the patient's position with respect to the axis of the x-ray beam can entirely eliminate. Body section roentgenography is the only roentgen method that can appreciably diminish this drawback, but this method cannot be used

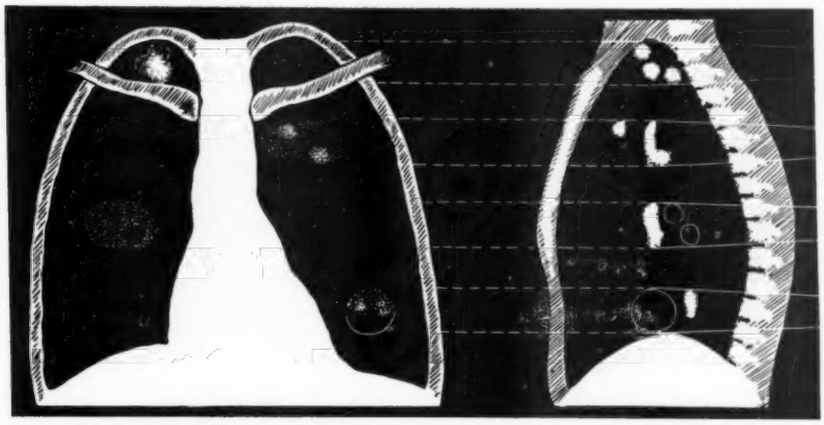

FIG. 1. Schematic drawing illustrating the summation and superimposition of radiopacities and radiolucencies in the roentgenogram. (Modified from Chaoul.)

routinely because of the prohibitive time-consuming and cost factors.

This problem of superimposition and summation of shadows becomes a severe handicap when we consider the lower limits of visibility of shadows in the roentgenogram.[1] It has been estimated that under optimal conditions a radiopaque shadow as small as 2 mm. in size can be discernible in the roentgenogram. It is extremely important to note that in this order of magnitude most of the finer structures of the lung, e.g., bronchioles with associated vascular and lymphatic vessels, connective tissue septa (alveolar, acinar or lobular walls) are much less than 2 mm. in thickness.[2] It is apparent therefore that the finer lung structures which are observed in the roentgenogram must be a summation of these "subvisible" or microscopic components to produce the finer lines, lacework or reticular pattern of radiopacity as contrasted with the air in the surrounding lung. In other words this roentgenographic picture depends on two variable factors which may act independently or concertedly, namely, the amount of air adjacent to the radiopaque structures and the thickness of these structures.

Furthermore, visibility, as it pertains to the roentgenogram, being a subjective phenomenon (obviously influenced by the training and past experience of the observer) is greatly dependent on the following additional factors: (1) status of the edges of the radiopacity, i.e., sharp, fuzzy, irregular; (2) density, i.e., presence of calcification (radiopacity being more easily discernible than radiolucency); (3) structure and configuration of the radiopacity, e.g., linear, tubular, mosaic, solid round, wedge, homogeneous; (4) technical and miscellaneous factors which include characteristics of x-ray machine, focus, object, films, distance, processing;

TABLE 1
CHARACTERISTICS OF ROENTGEN FINDINGS

I. Increased Densities (Radiopacities) (Fig. 2)	II. Decreased Densities (Radiolucencies) (Fig. 3)
A. Form and size 1. Linear 2. Miliary 3. Nodular (round or blotchy) 4. Segmental or lobar configuration 5. Contour (peripheral, mediastinal, diaphragmatic)	A. Form and size 1. Linear 2. Miliary (?) 3. Cyst-like or cavitary 4. Segmental (?) or lobar 5. Contour
B. Degree of density	B. Degree of radiolucency
C. Homogeneity or structural pattern	C. Structural pattern

D. Position and distribution (single or multiple)
E. Effects on adjacent area (changes in spatial relationships) (Fig. 4.)
1. Immediate local area
2. General thoracic structures
F. Additional information gleaned from special roentgen technics
1. Modification by physiologic maneuvers and changes in position
2. Special procedures
G. Roentgenographic evolution of the process (stationary, progressive or regressive)
H. Associated roentgen findings (thoracic or extrathoracic)

(5) patient characteristics of size, age, condition, thickness of thoracic wall.

It is not surprising, therefore, that not only is there a wide variation in the appearance of normal chest roentgenograms of different individuals, but also variations in appearance of the same individual's normal chest may occur when taken at various times under different conditions. Despite improvements in equipment and standardization many of the foregoing problems cannot be resolved in the foreseeable future.

In the absence of more definitive criteria we are obliged to rely upon the impressions and considered opinions of qualified individuals based on their controlled experience using the best technical facilities and a modicum of standardization.

DESCRIPTION OF ROENTGEN FINDINGS

Since no classification is available that is entirely satisfactory, we shall use certain descriptive roentgen characteristics as guide-posts for our discussion.[3] (Table 1.) Obviously a lesion can be manifested by just one roentgen finding or by a combination of several of these findings. It should also be noted that the superimposition of densities makes it difficult at times to characterize properly the roentgenographic appearance.

A. Radiopacities

1. Linear (streaks, bands, strands) (Fig. 2A): Roentgenographically there is a basic linear pattern in the lung fields which is essentially tree-like in distribution. This represents the normal lung structure for which the anatomic term bronchovascular markings is used. Abnormal linear radiopacities range from mere accentuation of the normal pattern to marked thickening and irregularity with superimposed streaks, bands or strands. These striae may be localized or widespread in distribution, vary in density, and conform to the usual arboreal lung structure or deviate markedly from it. If they extend to the periphery of the lung, they occasionally assume a fine reticular architecture. In some conditions transition phases exist between the linear and miliary radiopacities so that the boundary line between the two forms is not sharp. In the localized types the density in question may be a gradation from the linear to a disc or plaque-like form.

2. Submiliary, miliary and granular (Fig. 2B): These comprise densities which range in size from the just visible to a few millimeters in diameter. The lesions may be few or very numerous and typically widely distributed. They exist as individual lesions or as localized groups in cluster formation, which in turn are symmetrically or asymmetrically distributed. The size and density of the punctate shadows may be uniform or varied. Furthermore, they may be so poorly defined as to merge with the fine septal markings.

3. Nodular (Fig. 2C): These are divided into the more or less rounded lesions which are fairly well circumscribed, and the blotchy or patchy areas with ill defined margins. The size ranges from less than a centimeter to several centimeters in diameter. The lesions may be single or multiple, localized or widely scattered. The shadows may appear homogeneous or mottled, dense or hazy.

4. Conforming to a segmental or lobar configuration (Fig. 2D, 2E): Such lesions may be single or multiple, unilateral or bilateral. The edges may seem fuzzy or sharply delineated. Associated changes in spatial relationships of the intrathoracic structures sometimes occur. The degree of opacity varies from a hazy or ground-glass to a very dense appearance either homogeneous or mottled.

5. Peripheral contour (Fig. 2F): Included in this group are those lesions which border or involve the mediastinum, diaphragm or thoracic wall and which encroach upon or obscure the adjacent pulmonary field. These vary from a small localized density, for example in the costophrenic sinus or hilus, to a massive density involving an entire hemithorax. (Fig. 4A.) Frequently the edges of the shadows bordering on the lung field are sharply defined and have characteristic contours such as concavity, convexity, lobulation, etc. In other cases this "free" edge is poorly defined and appears serrated or brush-like.

B. Radiolucencies

1. Linear: Streaks of decreased density are projected through the lung fields when air escapes into the soft tissues of the chest wall as in subcutaneous emphysema. Radiolucent linear bands are also occasionally seen in such

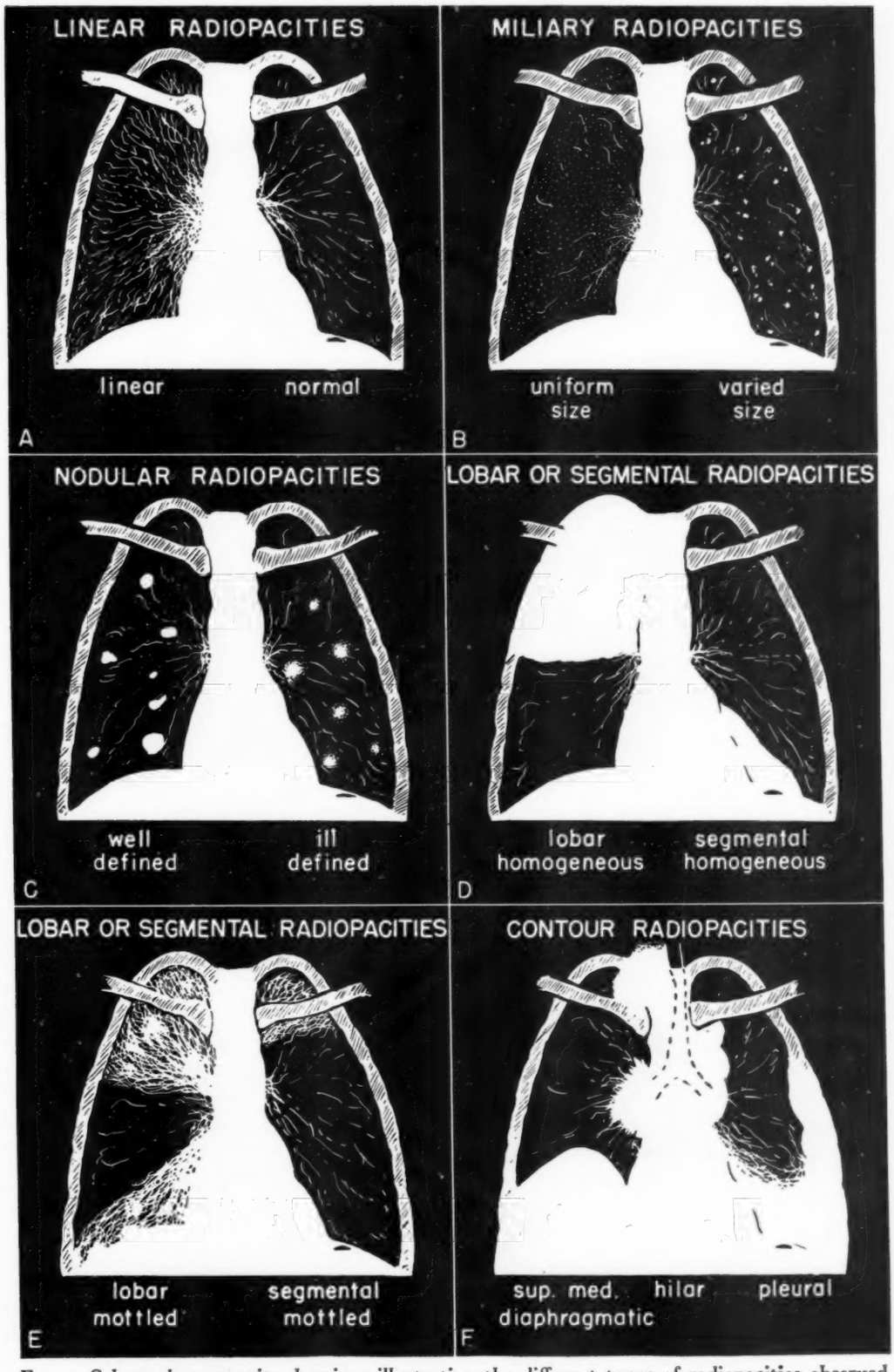

FIG. 2. Schematic composite drawings illustrating the different types of radiopacities observed in the roentgenogram.

conditions as cylindric bronchiectasis and consolidation.

2. Miliary(?) size: Such radiolucencies are theoretically possible and have been described, but for practical purposes no criteria exist for the roentgen differentiation from the normally aerated lung.

3. Cavitary or cyst-like (Fig. 3A, B and C): These lesions range from less than 1 cm. to several centimeters in diameter. They may be single or multiple, unilateral or bilateral and are practically always delinated by a surrounding radiodensity. Furthermore, the radiolucent zone itself may be homogeneously clear or traversed by linear or other radiopacities to form structural patterns of various types.

4. Conforming to a segment(?), lobe or entire lung (Fig. 4B to 4F): Except for the unusual cases of pulmonary embolism without infarction this finding is observed only in various types of emphysema. Frequently there are concurrent roentgen findings of changes in spatial relationships. Obstructive emphysema of a segment, although occurring pathologically, is seldom demonstrated on the roentgenogram because the changes are not obvious or because the overlying lung markings obscure the hyperaeration.

5. Peripheral contour (Fig. 3D to 3F): When adjacent to the thoracic wall, mediastinum or diaphragm, these lesions may take the form of sharp radiolucent zones of various widths or localized radiolucent pockets of various sizes and shapes, with or without fluid levels. They are invariably bounded by radiopacities as, for example, in peripheral pneumothorax the visceral pleura shows up as a very fine linear density forming the boundary of the collapsed lung.

C. Effects on Adjacent Area (Changes in Spatial Relationships (Fig. 4)

The mediastinum, diaphragm, thoracic wall and lungs possess varying degrees of pliability. Because of this property certain changes in spatial relationships of the thoracic structures occur whenever abnormal differences in intrathoracic pressure exist as a result of disease processes.

1. Immediate local area: The effect of a lesion on the immediate adjacent area may be nil or take the form of crowding or spreading of the adjacent linear lung markings and may be associated with decreased or increased radiolucency.

2. General thoracic structures: Changes in spatial relationships may be slight or very pronounced. In addition to changes in distribution of the lung markings over a wide area, the following changes may occur singly or in combination: increase or decrease in the thorcic or hemithoracic volume, widening or narrowing of the intercostal spaces and corresponding changes in the direction of the ribs, mediastinal shift, elevation or depression of the leaves of the diaphragm, displacement of the lung roots, displacement of the interlobar fissures.

D. Additional Information Gleaned from Special Roentgen Technics

These include (1) certain physiologic maneuvers such as forced respiratory movements[4] (Valsalva's and Muller's), coughing, sniffing, may change the roentgen appearance of the lesion in question and so aid in diagnosis. (For example, the Valsalva maneuver tends to decrease the amount of blood in the pulmonary vessels and so differentiation can at times be made between engorged vessels and masses in the lung roots.) (2) Changing the position of the patient, for example to the supine or apical lordotic or lateral recumbent, will often give valuable additional roentgen information. (3) Such special procedures as body section roentgenography, angiography, induced pneumothorax, stereoscopy or bronchography are often necessary to demonstrate the nature of the lesion which may not be apparent on the conventional roentgenograms.

E. Roentgenographic Evolution of the Process

The evolution of the roentgen finding can only be evaluated by follow-up roentgen studies or from previous roentgenograms; this is important and may, in fact, be decisive. Two features can be ascertained in these studies, namely, the stability of the lesion (whether stationary, progressive or regressive), and the time-change relationship (whether hours, days, weeks, months or years).

Since a definitive diagnosis cannot be made solely on the roentgen findings, correlation with pertinent clinical and laboratory data is imperative for proper analysis of the roentgenogram in order to confirm the initial impression or to arrive at a final diagnosis. This information may be summarized as follows: (1)

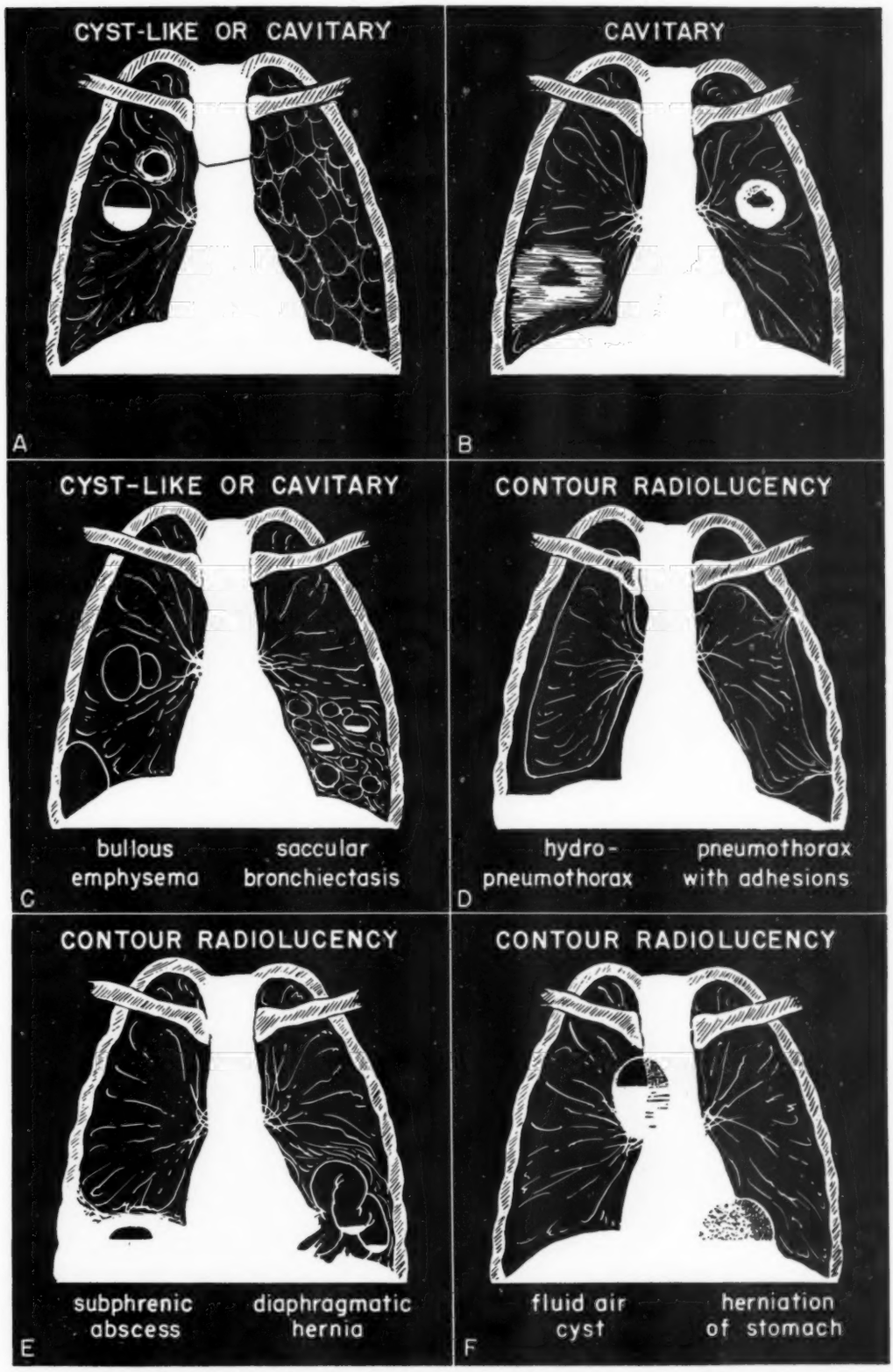

FIG. 3. Schematic composite drawings illustrating the different types of radiolucencies observed in the roentgenogram.

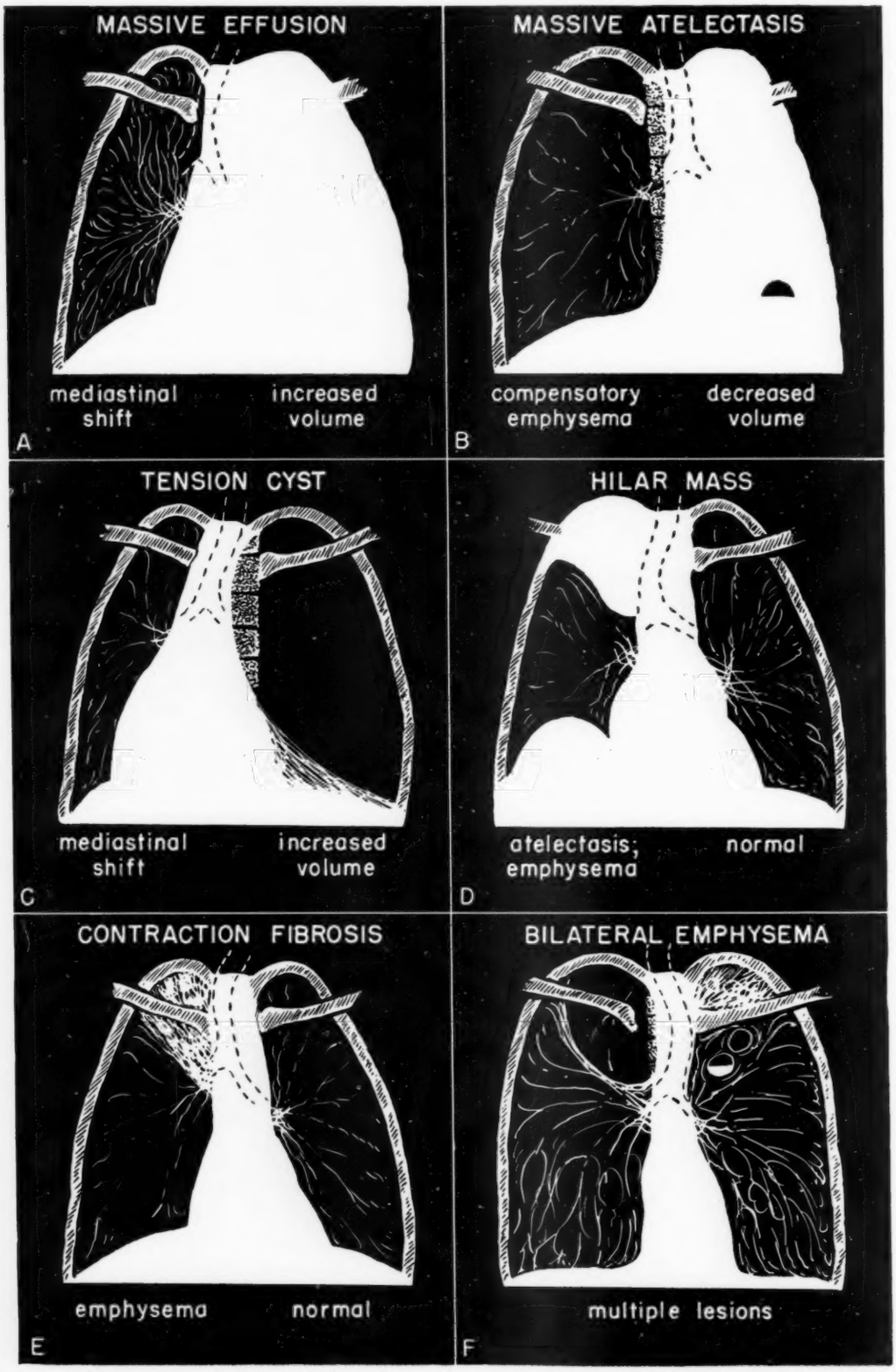

FIG. 4. Schematic composite drawings illustrating changes in spatial relationships and multiple lesions observed in the roentgenogram.

clinical history: exposure, geography, occupation, age, sex and race, and response to chemotherapy, and antibiotics; (2) clinical findings: pulmonary, extrathoracic, cardiovascular, respiratory functional studies; (3) sputum and bronchial secretions: smears, cultures, animal inoculation, cytologic studies; (4) gastric washings; (5) lymph node biopsy; (6) pleural fluid: cytology, bacteriology, type of fluid; (7) bronchoscopy: biopsy, aspiration; (8) blood studies: peripheral smear, bone marrow smear, culture, sedimentation rate, blood chemistry; (9) serologic and agglutination tests; (10) skin tests; (11) surgical procedures: induced pneumothorax, induced pneumoperitoneum, thoracoscopy, thoracotomy.

Obviously not all of this information is necessary or readily obtainable in every case. In some cases just a few additional facts may be sufficient to establish the diagnosis; in other cases even after exhausting the entire gamut of clinical procedures and laboratory tests a definitive diagnosis still cannot be made. In the majority of organic lesions the final diagnosis can only be made by pathologic study of the tissues.

LESIONS PRODUCING RADIOPACITIES

A. Linear Radiopacities

Inflammatory	Neoplastic lymphangitic spread
Acute bronchitis	Primary bronchogenic carcinoma
Measles, whooping cough, other viral disease	Metastatic neoplasm
Chronic bronchitis	Malignant lymphoma and leukemia
Cardiovascular	Storage diseases
Pulmonary hypertension	Collagen diseases
Passive pulmonary congestion	Idiopathic pulmonary fibrosis
Lung dusts (pneumoconiosis)	
Silicosis	
Asbestosis, etc.	

Accentuated linear radiopacities are due to the following factors which may act singly or more usually in some combination;[5] furthermore they may be a prelude to the development of other types of radiopacities. (1) Dilatation or engorgement of the pulmonary vessels; (2) interstitial or peribronchial inflammatory infiltration; (3) accumulation of bronchial secretions; (4) interstitial deposition of endogenous or exogenous foreign material; (5) lymphatic neoplastic infiltration; (6) dilatation or engorgement of the lymphatic vessels; and (7) interstitial and peribronchial fibrosis.

From a pathologic point of view, except for reversible cases, a sequel or common denominator of practically all the foregoing conditions is a greater or lesser degree of fibrosis involving the interstices of the lung. Distribution, location, extent and age of the fibrosis along with the invariably associated emphysema, atelectasis, bronchiectasis and disturbance of pulmonary circulation add to the complexities of the roentgenogram. Those cases in which the fibrosis has no known etiology have been termed idiopathic pulmonary fibrosis.

Linear radiopacities in themselves are usually insufficient to explain the underlying pathologic process; but when coupled with other associated roentgen and clinical findings, a basis for differential diagnosis is established. The following comments are made with this in mind.

1. Dilatation or engorgement of pulmonary vessels: (1) Active pulmonary congestion: In acute inflammatory conditions the pulmonary vessels dilate or become engorged. In mild cases these changes may be insufficient to produce recognizable changes in the roentgenogram, e.g., in cases of acute bronchitis the roentgenogram of the chest frequently is within normal limits. However, in more severe cases or in progressive cases, engorgement frequently leads to exudation into the interstitial tissues, termed by some authorities peribronchial infiltration. (2) Pulmonary hypertension: In pulmonary hypertension due to primary pulmonary arteriosclerosis or secondary to lung parenchymal lesions as emphysema or fibrosis, there is enlargement of the hilar vessels as well as the arterial branches radiating into the lung fields resulting in accentuation of the lung markings. As a rule, the hilar prominence due to the dynamically dilated pulmonary vascular roots is sharply defined in contradistinction to passive pulmonary congestion where the edges are indistinct. (3) Passive pulmonary congestion: This is basically due to increased pressure in the pulmonary veins, e.g., cardiac disease. Associated roentgen findings such as enlarged heart with or without characteristic pathologic configuration will help in the diagnosis.

2. Interstitial or peribronchial inflammatory infiltration: (1) Acute inflammations involving primarily the interstitial tissues, e.g., as atypi-

cal, viral or interstitial pneumonia, cause increased markings because of the accumulation of inflammatory exudates in the interstitial tissues and are usually associated with miliary or larger densities. (2) In more chronic inflammatory conditions such as bronchitis, the accentuation of the markings is due not only to interstitial inflammatory infiltration but also interstitial or peribronchial fibrosis; furthermore the findings are altered by superimposition of other conditions such as emphysema and bronchiectasis.

3. *Accumulation of bronchial secretions:* Replacement of air in the bronchial tubes by secretion produces increased linear densities. Alveolar filling and atelectasis may occur as sequelae.

4. *Interstitial deposition of endogenous or exogenous substances:* This is observed in hemosiderosis, storage diseases and pneumoconiosis. In the early stages it is problematical whether the deposit or the associated fibrosis is the cause of the increased linear densities. In cases such as silicosis the accentuation of the linear markings is seen only in the early phases of the disease; the evolution is usually progressive and leads to further fibrosis and obstructive phenomena manifested by additional radiopacities and radiolucencies. These cases are frequently susceptible to superimposed acute or chronic infection or tuberculosis which adds to the roentgen findings. With less innocuous dusts, e.g., siderosis, the fibrosis may be minimal and not necessarily progressive, and in these cases the roentgenograms show, in addition to a fine reticular linear pattern, superimposed punctate densities which are apparently primarily due to the deposited material rather than the fibrosis.

5. *Lymphatic neoplastic infiltration:* Malignant cells may infiltrate lymphatics and occasionally produce linear radiopacities radiating outward from the hilus to the periphery of the involved segment, lobe or lung, as in primary bronchogenic carcinoma, metastatic carcinoma (of stomach, breast, etc.), malignant lymphomas and luekemias. Subsequently small nodular infiltrations make their appearance along the thickened streak densities. Associated roentgen findings, for example a primary lesion outside the chest or involvement of the osseous system, may help in the diagnosis.

6. *Dilatation or engorgement of the lymphatic vessels:* Many of the conditions described previously can lead to engorgement of lymphatic channels and stasis of lymphatic flow. These engorged vessels are best seen in the peripheral portions of the lung bases and are not consonant with the normal linear markings.

B. Single or Few Radiopaque Strands and Plaques

Included here are linear streaks or band-like radiopacities which are few in number, more localized in character and do not conform to the normal bronchovascular markings. Very often the previous history or evaluation of preceding roentgenographic findings will determine the original cause of the linear radiopacity. The pathologic examination of these bands, especially if fibrotic frequently cannot divulge the nature of the original lesion. These usually fall into three groups:[6] (1) *Focal, disc or plaque-like atelectasis* due to stenosis or plugging of small bronchi. This produces radiopaque bands running parallel with the bronchovascular markings. They are single or multiple and are most frequently located in the bases. They may be reversible and rapidly transient or irreversible as a result of organization and fibrosis. (2) *Fibrous scars* following granulomatous lesions, suppurations or infarcts. These also are manifested by radiopaque streaks or bands or lines and may be localized in any part of the lung. (3) *Localized pleural bands and thickenings* such as thickened interlobar fissures, peripheral pleural thickening, pericardial, diaphragmatic and mediastinal pleural adhesions as the result of inflammatory processes. The nature of these lesions can be frequently ascertained on the roentgenogram from their location or from their peaked or tent-like configuration.

C. Submiliary, Miliary, Granular Radiopacities

Inflammatory	Lung dusts (pneumoconiosis)
Miliary tuberculosis	Neoplastic
Bronchiolitis	Miliary carcinomatosis
Lobular bronchopneumonia	Malignant lymphoma and leukemia
Viral or atypical pneumonia	Pulmonary adenomatosis
Mycoses	Sarcoidosis
Tularemia	Storage diseases
Cardiovascular and renal	
Interstitial or lobular edema	

The underlying pathologic process is due to either of the following, singly or in combination: (1) Interstitial accumulation or deposition of fluid, inflammatory products, foreign substances or neoplastic cells. (2) Alveolar involvement (from several alveoli to groups of acini) by filling with fluid, inflammatory products or neoplastic cells, or by loss of air content, or by a combination of both, e.g., lobular or capillary bronchopneumonia, lobular atelectasis.

Both processes give rise to radiopacities in the range of several millimeters and their size or distribution alone cannot determine which of these two types is present. This interstitial or aveolar phase may progress to a more advanced stage with small patchy nodules or even larger segmental or lobar blotchy radiopacities. In miliary carcinomatosis the radiopaque foci are usually of different sizes apparently the result of multiple metastatic episodes. On the other hand, in miliary tuberculosis there is a tendency toward uniformity in size and density of the radiopacities. Other associated roentgen findings will often suggest the diagnosis, e.g., in sarcoidosis a bilateral hilar lymphadenopathy is frequently present which is usually quite evident on the roentgen examination; in mitral stenosis there are characteristic changes in the cardiac silhouette and hilar enlargement from vascular engorgement.

D. Nodular (Round or Blotchy) Radiopacities

Solitary	Multiple
Inflammatory	Inflammatory
Tuberculoma	Tuberculosis
Mycoses	Bronchopneumonia
Lung abscess	Lung abscesses
Neoplastic malignant	Mycoses
Primary peripheral carcinoma	Neoplastic malignant
Malignant lymphoma	Metastatic
Metastatic neoplasm	Malignant lymphomas
Pleural tumor	Pulmonary adenomatosis
Neoplastic benign	Cardiovascular and renal
Hamartoma, etc.	Lung infarcts
Fluid cyst	Arteriovenous fistula
Parasitic	Pulmonary edema
Congenital	Fluid cyst
Cardiovascular	Parasitic
Infarction	Congenital
Arteriovenous fistula	Multiple atelectasis
Small encapsulated pleural fluid	Lung dust diseases
Fibrin body	Blast injuries
Chest wall lesions	Irritating vapors or gases

While there are many exceptions, the acute inflammatory conditions and pulmonary edema are usually blotchy in configuration or have ill defined edges. The chronic inflammatory, granulomatous or lung dust diseases may be either well defined or poorly defined. The primary peripheral and secondary metastatic malignant lesions, fluid cysts, as well as encapsulated interlobar effusions are more apt to be well circumscribed.

1. Tuberculoma: Tuberculomas include the "healed" peripheral initial lesions of tuberculosis, inspissated tuberculous cavities and inactive reinfection foci.[7] In all these cases the shadow is fairly well circumscribed and spheroidal or oval in configuration. For the most part tuberculomas are clinically silent and found on routine roentgen examination in any portion of the lung fields. Calcification is frequently present but may be very minimal in extent.

As a general rule the presence of calcification in intrathoracic lesions indicates benignity.[8] A distinction, however, must be made between calcification in a pathologic specimen and so-called "calcific density" observed in the roentgenogram. In cases in which the calcification is extensive there is rarely any question, however, minute areas of pathologic calcification may be obscured or missed radiologically even with special technics such as spot views, bucky technic or body section roentgenography. On occasion densities simulating calcification may be produced by other substances, as in lung dust diseases. It might also be mentioned here that occasionally carcinoma of a retrosternal thyroid may be calcified, or malignant tumors invading the mediastinum may surround and incorporate old calcified hilar or mediastinal lymph nodes giving the impression of being calcified.

2. Mycotic infections: Except for cases of coccidiomycosis and histoplasmosis in endemic areas mycotic lesions are rare. The occurrence of a single nodule is extremely rare. The mycotic infections may mimic any number of pulmonary diseases especially tuberculosis, not only radiologically but clinically as well. Therefore the final diagnosis depends on laboratory studies.

3. Benign or malignant neoplastic nodules: Most benign neoplasms unless calcified, e.g., hamartoma, have no characteristic radiologic or clinical findings which are distinctive and the

final diagnosis depends on pathologic studies. Benign or malignant nodules may have various forms such as spheroidal, ovoid or lobulated. In the case of secondary metastatic neoplastic nodules there is no characteristic radiologic finding which will indicate the site or type of the primary tumor. In the evolution of these diseases the growth may be slow or rapid and other nodules may make their appearance. The so-called peripheral lung carcinoma shows no features distinguishing it from other solitary nodular lesions. The condition termed pulmonary adenomatosis, as distinguished from the single peripheral type of primary nodular carcinoma, is usually multiple and shows a relatively slow growth with eventual coalescence of the nodules to involve large areas of the lung; although it simulates repeated episodes of chronic pneumonitis the presence of copious watery sputum in the later stages suggests the diagnosis.[9] Malignant lymphomas occur very rarely as single nodules and only occasionally as multiple nodules.

4. Cysts: Parasitic infestation such as the ecchinococcus is rare in the United States. There frequently is peripheral calcification of the cyst. The presence of satellite cysts may produce more distinctive findings.

Congenital fluid lung cysts are usually sharply defined although, if infection supervenes, a fuzzy outline results. The shape of the cyst may change with change in position of the patient and with respiration.[10] There are no other characteristic roentgen findings. The final diagnosis depends on the pathologic study of the wall of the cyst.

5. Pulmonary infarct: The size and shape of the infarct varies. Despite the frequently described typical wedge-shape, the roentgen findings seldom demonstrate this configuration. The infarct is usually associated with some pleural reaction although this may not always be evident in the roentgenogram. Over a period of time infarcted areas show a slow, gradual decrease in size until either resolution occurs or scar replacement results. Infarcts may be multiple in cardiac failure, or from embolic phenomena. Superimposed congestion, pulmonary edema and infection usually obscure the infarcts and make roentgen diagnosis difficult or impossible.

6. Pulmonary arteriovenous fistula: Under favorable conditions the fistula shows changes in size during the Valsalva and Muller maneuvers. This may be solitary but it usually appears as a conglomeration of round shadows and sometimes there is an obvious vascular connection with the hilar vessels. The common site is in the lung base. A definitive diagnosis may be made by angiocardiography.

7. Fibrin bodies: Fibrin bodies are usually associated with hydropneumothorax and may at times be confused with lung nodules.

8. Encapsulated pleural fluid: Occasionally small collections of pleural fluid, especially in the interlobar fissures, have a shape that simulates an intrapulmonary nodular lesion. Special views such as the lordotic or lateral recumbent, and also body section roentgenography will help to locate the lesion in the pleura.

9. Pulmonary edema: Pulmonary edema may occur in blotches or ill defined areas in both bases or dependent areas. In more advanced cases these blotchy areas coalesce into diffuse. mottled densities which at times assume a characteristic "butterfly" appearance adjacent to the hila in the inner two-thirds of the lung fields, the peripheral lung fields remaining well aerated or relatively uninvolved. Irritating gases or vapors may result in blotches of radiopacities in both lung fields as in pulmonary edema.

10. Pneumonias: Many of the problems of inflammations of the lung which were never satisfactorily resolved within the field of pathology have been carried over in part or whole to the field of roentgenology. Frequently infection and inflammation are used as synonymous terms, and such terms as atypical pneumonia, radiation or allergic pneumonitis are often misused because no roentgen or pathologic criteria exist for their diagnosis. Furthermore, the terms pneumonitis or interstitial pneumonitis have certain connotations but no sharp boundaries separating them from other inflammations of the lung, and to use these terms in radiologic language further confuses the nomenclature. The situation becomes worse when specific etiology, as viral or bacterial, is coupled with roentgen diagnosis.

In smaller lesions roentgen differentiation between inflammatory exudation, edema or atelectasis is often impossible. In addition the superimposition or summation of numerous shadows simulates confluency or coalescence when such is not the case. Oblique or other views can seldom resolve this difficulty. Therefore, it is best to describe as accurately

as possible the roentgen findings as to location, extent, size and shape or configuration without attempting, in smaller lesions, to denote underlying pathology as pneumonia, or small anatomic structures as lobules or acini. Follow-up roentgen studies or evolutionary appraisal of the process can further aid the clinician by noting complications as obvious atelectasis, cavity formation or pleurisy.

In atypical pneumonia there are blotchy radiopacities which pathologically are assumed to consist of areas of interstitial or alveolar exudation, edema and atelectasis. This includes a large miscellaneous group of pulmonary infections due to viral, bacterial or unknown etiology.

Loeffler's syndrome is supposedly an allergic pneumonitis of non-infectious nature. It shows evanescent patches or blotches of radiopacity associated with increased eosinophils in the blood and sputum and few or no clinical symptoms. These blotches do not conform to bronchopulmonary segments and are believed to be edematous areas.

In some cases of acute inflammatory processes even though the alveoli are still not flooded with exudate the presence of pleural pain may reflexly or otherwise interfere with proper respiratory movements and aeration of the lung, particularly of the basal segments. This results in hypoaeration of these segments which further reduces the radiolucency and contrast of the pulmonary fields.

E. Radiopacities Conforming to Segmental or Lobar Configuration

Inflammatory	Atelectasis associated with fibrosis
Atypical or viral pneumonia	Bronchiectasis
Coalescent bronchopneumonia	Tuberculosis
Lobar pneumonia	Atelectasis, obstructive
Pulmonary abscess	Bronchial mucus plugs, edema, etc.
Tuberculosis	Inflammatory stricture, granulation tissue
Mycoses	Neoplasm
Malignant neoplasm	Cardiovascular
Primary carcinoma	Pulmonary edema
Pulmonary adenomatosis	Pulmonary infarction
Malignant lymphomas	

Densities of segmental or lobar configuration are due to filling of the air spaces with fluid, inflammatory products or neoplastic cells, or are due to atelectasis. Various combinations of both alveolar filling and atelectasis can occur. While pathologically there is usually no difficulty in differentiating areas of exudation or edema from atelectasis, the roentgen differentiation may be very difficult or impossible unless definite decrease in volume is demonstrable in the roentgenogram.

If there is uniform filling of all the alveoli in a bronchopulmonary segment or lobe, there is no appreciable change in volume and the roentgen density produced is homogeneous. e.g., pneumococcal lobar pneumonia. Since the introduction of the sulfanilamides and antibiotics this type of consolidation is only occasionally observed on roentgenographic studies.

When there is unequal or irregular filling of the alveoli interspersed with groups of well aerated alveoli, there is again no appreciable change in volume of the affected portion of the lung, however, the roentgen density produced is heterogeneous or mottled, e.g., coalescing bronchopneumonia.

Should there be unequal or irregular filling of the alveoli interspersed with groups of well aerated and groups of atelectatic alveoli, again there is a mottled density produced; however, there is also a variable decrease in volume of the involved segment or lobe, e.g., in bronchial adenoma the nature of the obstruction is such that it leads to a variable degree of atelectasis associated with infection.

If there is uniform atelectasis of all the alveoli in a bronchopulmonary segment or lobe, a dense homogeneous radiopacity results with a definite decrease in volume of that portion of the lung, e.g., rapidly developing complete bronchial obstruction from any cause. Since in practically all types of obstructive atelectasis there is some alveolar fluid present, it is obvious that the amount of fluid will determine the extent of the decrease in volume. This accounts for the terms dry or wet atelectasis to imply amount of fluid present.

In chronic inflammatory conditions, in addition to the factors discussed previously, there is also a variable degree of fibrosis with contraction of the involved area producing a mottled radiopacity with decrease in volume of the segment or lobe. These changes are associated with bronchiectasis. Although the term

bronchiectasis by definition signifies merely dilation of the bronchi, the medical usage usually implies the secondary addition of infection with inflammatory and fibrotic changes involving not only the components of the bronchial wall but also the adjacent lung. Here the dilation is irreversible. The associated pulmonary changes are frequently marked but may be minimal in some stages of bronchiectasis. The roentgenogram in the latter cases may appear essentially normal.

F. Contour Radiopacities Bordering the Thoracic Wall

Pleural effusion	Pleural tumor
Inflammatory	Pleural thickening
Tuberculosis	Lesions of the chest wall
Pneumonia	Inflammatory
Subphrenic abscess	Tumors
Cardiovascular or renal	
Heart failure	
Azotemia	
Neoplastic	
Metastatic	
Primary	
Traumatic	

1. Pleural fluid: The nature of the fluid cannot be determined radiologically. Depending on the amount of fluid, the roentgen appearance ranges from a thin ribbon-like radiopacity along the lateral chest wall with partial obliteration of the normal costophrenic sinus, to a marked radiopacity of practically the entire hemithorax with displacement of the heart and mediastinum toward the sound side. The degree of shift of the mediastinum is influenced by the presence or absence of underlying obstructive atelectasis or by mediastinal fixation. In massive pleural effusion the conventional roentgenogram shows a characteristic curvilinear superior border to the free margin of the radiopacity provided there is no air in the pleural space. Once air is introduced into the pleural cavity a horizontal air-fluid level will be visible only if the central roentgen ray is parallel to the level. By changing the position of the patient with respect to the axis of the central ray, the pleural fluid, with or without the presence of air in the cavity, confers a diffuse haziness over the entire hemithorax in the roentgenogram with a loss of the characteristic curvilinear or linear boundaries. Loculation of the pleural fluid prevents mobility and the fluid then assumes various shapes from round or oval to bizarre configurations with frequent extensions into the fissures. Loculated fluid may appear flattened against the adjacent thoracic wall.

2. Tumors of the pleura: Pleural neoplasms give rise to abnormal, dense, peripheral contours at times suggesting nodular or massive shadows. The exact location of these nodules or masses on the pleural surface or in the periphery of the lung can usually be determined by special tangential views. Usually pleural fluid is present and thoracentesis is necessary either with or without the introduction of air to uncover the pleural masses.

3. Pleural thickening: This may vary from a thin dense band simulating a small amount of fluid to marked thickening with contraction of the entire hemithorax producing in the roentgenogram a veiling, hazy effect over the entire lung field. The frequently present underlying pulmonary pathology may be partly or completely obscured.

4. Thoracic wall lesions: Localized inflammatory or neoplastic lesions of the skin, ribs and soft tissues appear radiographically as round or oval densities sharply demarcated or ill defined. By proper projection their peripheral origin can usually be ascertained.

G. Contour Radiopacities Bordering the Diaphragm

High position	Abnormal contour
Right-sided eventration	Fluid
Right-sided paralysis	Tumor
Subphrenic disorder	Tenting
Herniation of solid viscus	Mammillation

Accumulations of pleural fluid or inflammatory products, although uncommon, do occur on the diaphragmatic surface and the contour may be irregular or smooth. The radiopacities produced are often indistinguishable from a high diaphragm or from subdiaphragmatic solid densities. Pleural fluid between the lung base and the diaphragm need not be encysted and in such cases may flow to other parts of the hemithorax with change in the position of the patient. In cases of subphrenic abscess, in addition to elevation of the diaphragm, the roentgenograms also show some fluid in the costophrenic angle on the same side; later a gas shadow with a fluid level may make its

appearance below the diaphragm. Tumors of the diaphragm are rare; induced pneumothorax or pneumoperitoneum will help to differentiate them from mammillation, herniation, basal pulmonary tumors and subdiaphragmatic tumors.

H. Contour Radiopacities Bordering the Mediastinum

- Anterior Mediastinum
  - Retrosternal thyroid
  - Thymic enlargement or tumor
  - Teratoma
    - Benign-dermoid
    - Malignant
  - Malignant lymphoma
- Middle Mediastinum
  - Inflammatory
    - Primary tuberculosis
    - Mycoses
    - Infectious mononucleosis
    - Other acute and chronic infections
  - Cardiovascular
    - Passive pulmonary congestion
    - Pulmonary hypertension
    - Congenital heart disease
  - Malignant Neoplasm
    - Lymphomas
    - Bronchogenic carcinoma
    - Secondary metastatic
  - Lung dust diseases
  - Sarcoidosis
- Posterior Mediastinum
  - Tumors of nerve tissue
  - Cysts
    - Bronchial
    - Gastroenterogenous
  - Esophagus—achalasia
  - Spine
    - Inflammation
    - Tumors
    - Marked deformities
- Lesions occurring in any mediastinal division
  - Aneurysms
  - Loculated mediastinal fluid

Many lesions of the mediastinum often give similar shadows which produce mediastinal widening or encroach on either or both lung fields. The position of the lesion in the mediastinum is helpful in the differential diagnosis. The mediastinum, for the purpose of this discussion is divided into anterior, middle and posterior divisions as follows: the region of the hilus and heart form the middle mediastinum; the region anterior to the heart and trachea is designated the anterior mediastinum; the region posterior to the heart and trachea is designated posterior mediastinum. Some pathologic conditions which apparently originate in one mediastinal division may extend into an adjacent division. Furthermore there are disease processes which may be found in any of the divisions.

1. *Anterior mediastinum:* Masses in the anterior mediastinum are usually well demarcated and for the most part benign. Substernal thyroid usually shows some compression effect on the trachea and may be partly calcified. Unlike other mediastinal masses in this region the retrosternal thyroid may move synchronously with the trachea on deglutition. Thymic enlargement is primarily a problem in children; characteristic configuration of sail-like shadows and effect on the trachea may be helpful. In adults the rare thymoma may occur anywhere in the anterior mediastinum; this lesion may be benign or rarely malignant. Dermoids are usually rounded, however, they may occasionally be irregular or lobulated in appearance; the periphery or the inner mass is frequently calcified; they may contain formed elements such as teeth, and fatty substances may give a layering effect. Other teratomas are occasionally malignant. Pericardial cysts are rare and usually are located in the cardiophrenic region.

2. *Middle mediastinum:* Since the size and configuration of the normal hilus and contiguous mediastinum offer a wide range of expression, obviously the borderline between normal and abnormal is wide and indefinite. This is conducive to the radiographically silent development of lesions in this region. A great many pathologic conditions (e.g., inflammatory, cardiovascular, neoplastic, dust disease) produce hilar vessel engorgement and/or mediastinal, paratracheal and bronchopulmonary lymphadenopathy; however, these changes frequently do not produce any recognizable abnormal hilar shadows. In most malignant lesions, by the time obvious shadow differences are recognizable, the lesion is already far advanced.

Enlargement of the hilus due to marked dilatation of the major pulmonary vessels frequently simulates hilar mass or lymphadenopathy; changes in the cardiac silhouette and in the vascular pattern in the pulmonary fields will usually clarify the situation.

Lymphadenopathy may cast a very slight or indefinite shadow, or at the other extreme, may produce large lobulated masses which project unilaterally or bilaterally from the mediastinal surface onto either or both lung fields. The mediastinal pleura overlying the enlarged lymph nodes or other mediastinal lesions may have smooth well-defined edges, but if the inflammatory or neoplastic process penetrates the lymph node capsule and mediastinal pleura it may invade and extend into the adjacent lung giving radiating or irregular margins to these shadows.

There are several important differential points in the diagnosis of obvious hilar lymph

node enlargement.[11] In children the most common cause is primary tuberculosis, whereas other conditions are uncommon. On the other hand, in adults malignant lymphomas, especially Hodgkin's disease predominate; these lesions may be unilateral or bilateral and when bilateral the enlargement is usually asymmetric. Obvious hilar lymph node enlargement in reinfection tuberculosis is rare, although calcified tuberculous nodes are very common. Sarcoidosis shows bilateral fairly symmetric hilar involvement; rarely are such nodes calcified. In silicosis gross hilar node enlargement may be extensive; the nodes may be calcified and may at times be of the egg-shell type. In addition there are extensive parenchymal changes in silicosis. Bronchogenic carcinoma as a cause of obvious hilar lymph node enlargement without other lung parenchymal signs is rare. Carcinoma of the esophagus as a cause of obvious hilar lymph node enlargement is very rare.

3. *Posterior mediastinum:* (1) Tumors of nerve tissues are paravertebral in location and sharply demarcated. Pressure erosion in the region of the intervertebral formina or pedicles may occur. Usually nerve tumors are benign and slow growing. (2) Congenital bronchial or gastroenterogenous cysts are uncommon. The bronchial cysts are parahilar in location or in the posterosuperior aspect of the mediastinum. Such cysts are usually well delineated. They may occasionally connect or communicate with the bronchial tree or gastrointestinal tract in which case lipiodol or barium studies may be of help. (3) In esophageal achalasia the markedly dilated, redundant, fluid-filled esophagus frequently projects to the right simulating a large tumor; barium studies reveal the nature of the lesion. Parenthetically, it is a good general rule in all suspected mediastinal lesions to study the esophagus with the aid of a barium meal. (4) The problem of deformities and other lesions of the spine which simulate mediastinal contour radiopacities can usually be resolved by proper roentgen studies of the spine.

4. *Lesions occurring in any mediastinal division:* (1) Aneurysms are found in any segment of the thoracic aorta but are most frequent in the ascending portion and arch. Calcification is found in both leutic and arteriosclerotic varieties although when found in the ascending aorta they are more probably syphilitic in nature. Angiocardiography may be necessary for differential diagnosis from mediastinal masses. (2) Loculated mediastinal fluid may occur anteriorly or posteriorly. Such cases are difficult to differentiate from mediastinal masses. If air is also present it offers the same diagnostic problems as gas-fluid pockets in other parts of the chest.

LESIONS PRODUCING RADIOLUCENCIES

A. Radiolucent Streaks and Bands

1. *Subcutaneous emphysema:* In subcutaneous emphysema the air is projected through the lung fields and appears as radiolucent streaks. These streaks do not conform to the normal lung architecture and are also visible in the soft tissues of the lateral chest wall and cervical region.

2. *Bronchi under certain conditions:* In some cases of cylindric bronchiectasis with pneumonitis or certain cases of consolidations in which the bronchi remain patent, radiolucent bands may be discernible because of contrasting densities between the air-containing bronchial lumina and the thickened bronchial wall with surrounding inflammation. Obviously the bronchial lumina more frequently are not discernible because of retained secretions or inflammatory products.

B. Caritary or Cyst-like Radiolucencies

Inflammatory cavitation	Saccular bronchiectasis
Lung abscesses, gangrene	Vesicular emphysema
Suppurative bronchopneumonia	Bullae, blebs, pneumatoceles
Friedlander's pneumonia	Air cysts
Tuberculosis	Congenital
Mycoses	Echinococcus
Infarction with cavitation	
Neoplastic cavitation	
Bronchogenic	
Hodgkin's	

1. *Cavitation:* The underlying pathologic process is always a necrosis of tissue which appears radiopaque until the necrotic material is evacuated through the bronchial tree at which time it acquires a radiolucent appearance. The radiolucent zone is associated with some surrounding contrasting pathologic process, the external boundary of which may be sharply circumscribed or diffusely hazy and of variable thickness. The inner boundary is either regular or irregular in outline and may have a characteristic horizontal gas-fluid level. Should the

cavity refill completely it will again appear radiopaque. Cavitation, single or multiple, can occur in many conditions and the differential diagnosis among septic, tuberculous or neoplastic lesions may be difficult.

2. *Saccular bronchiectasis:* This may be congenital or acquired, unilateral or bilateral and may involve a segment, a lobe or an entire lung. The saccules when empty appear as multiple cyst-like radiolucent spaces surrounded by various degrees of radiopacities as a result of peribronchial inflammation and fibrosis. These same saccules may appear as solid nodular radiopacities in the midst of mottled densities or have gas-fluid levels depending on the amount of retained secretions.

3. *Vesicular emphysema (focal emphysema):* On occasion during resolution of pneumonia or bronchial infections, especially in children, temporary, partial block of the smaller bronchi occurs leading to transient and reversible, single or multiple foci of obstructive emphysema which have the appearance of cyst-like or vesicular radiolucencies within the area of clouding.

4. *Blebs, bullae and pneumatoceles:* These are thin-walled radiolucencies which rarely contain fluid and are associated with pulmonary fibrosis. Depending upon their number and distribution and the condition of the surrounding lung parenchyma, these radiolucencies assume a round, oval, pyramidal or polyhedral configuration. The mechanism of their production is apparently on the basis of obstructive emphysema. Overlying lung parenchyma may partially obscure these radiolucencies. Occasionally the condition is progressive with the development of "vanishing lung." In large pneumatoceles the involved portion of the lung is increased in volume and the adjacent lung shows crowding of the bronchovascular markings; and if the pneumatocele is very large, there may be changes in spatial relationships of the entire hemithorax or chest.

5. *Congenital lung air cysts:* Those fluid cysts which communicate with the bronchial tree or pleural cavity may be partially or completely evacuated producing a radiolucent zone usually with a well defined wall. If the wall is very thin, an air cyst cannot be differentiated from a bulla or a pneumatocele radiographically. If the cysts become infected, the radiologic appearance is such that they cannot be differentiated from abscess cavities.

6. *Echinococcus cyst:* The echinococcus cyst may partially evacuate into a bronchus to produce a gas-fluid level configuration. Proper examination of the evacuated material will reveal the pathognomonic scolices.

C. Radiolucencies Conforming to a Segment(?), Lobe or Entire Lung

These include obstructive emphysema, compensatory emphysema, bilateral emphysema and pulmonary embolism without infarction.

The term emphysema simply signifies overinflation and dilatation of the pulmonary alveoli. This implies that there must exist criteria for: (1) normal alveolar size, from the microscopic point of view; (2) normal intra-alveolar pressure, from the functional point of view; (3) normal gross appearance, from the pathologic or radiologic point of view. Unfortunately such criteria are not too well defined.

Radiologically the essence of the definition, i.e., overinflation of alveoli, can only be expressed by the concept of increased radiolucency. However, the degree of radiolucency is only a subjective impression which is difficult to measure roentgenographically. Furthermore, the degree of radiolucency depends on such variables as patient characteristics and x-ray technical factors as mentioned previously. In addition, other associated pulmonary, pleural or cardiovascular changes may decrease or even obscure the radiolucency. The associated changes in spatial relationships of the thoracic structures, although very important for the diagnosis of emphysema, are also difficult to evaluate except in extreme cases.

Such descriptive terms as compensatory emphysema or senile emphysema are very often misnomers or have no suitable criteria. For example, compensatory emphysema obviously does not signify a physiologic compensation.[11] Here there is purely a physical rearrangement of distensible lung as a result of changes in intrathoracic or intrapulmonary pressure. It is conceivable that this overdistention may actually decrease the physiologic efficiency of the involved portion of the lung.

With these points in mind it is not surprising, therefore, to find marked discrepancies in the correlation of the clinical, pathologic and roentgen findings in problems of emphysema.

1. Obstructive emphysema: A most important condition causing radiolucency or hyperaeration of a lobe or lung is emphysema due to partial bronchial obstruction by means of a ball-valve type of mechanism. Both inspiratory and expiratory films may be needed to demonstrate this finding. In pronounced cases of unilateral obstructive emphysema the expiratory film is much more informative showing a definite increase in the radiolucency of the obstructed lobe or lung, depression of the ipsilateral diaphragm and a shift of the mediastinum toward the sound side. In bronchial obstruction of this type the series of events starts with slight emphysema and then progresses to pronounced emphysema. From this point of maximum hyperaeration there is a gradual or rapid loss of air, eventually leading to obvious atelectasis of the obstructed lobe or lung. The site and degree of obstruction may be relatively easy to determine only at both extremes of emphysema and atelectasis. The transitional phases between these two extremes may be very difficult or impossible to evaluate either as to site or degree of obstruction even with films taken on inspiration and expiration.

2. Compensatory emphysema: Secondary to fibrotic contraction of one hemithorax, massive obstructive atelectasis or surgical resection of a substantial portion of lung tissue, the contralateral lung distends and becomes hyperaerated. This ballooned lung may even extend across the midline into the opposite hemithorax. If the atelectasis or fibrotic contraction is localized to a segment or lobe, the adjacent or surrounding lung may show increased radiolucency as a result of physical rearrangement; this may be less definitive or obvious than in the case of involvement of an entire lung.

3. Bilateral emphysema: Without discussing the types or mechanism of development, obvious bilateral hyperaeration shows an increase in the radiolucency of both lung fields with or without increase or decrease in the lung markings. Increase in the volume of the thorax and depression of both leaves of the diaphragm are frequent accompaniments. The increased radiolucency is apparently due to some loss of parenchymal lung tissue (including a decrease of the vascular bed) coupled with an increase in the air content of the lungs. As a result of these changes plus a decrease in the systemic venous return the heart assumes a more elongated and narrowed configuration which obscures the frequently present right ventricular enlargement.

4. Pulmonary embolism without infarction: A radiolucent segment or lobe is possible when large emboli involve branches of the pulmonary artery without infarction. The mechanism apparently involves the plugging of the major vessels near the hilus with emptying of the blood from its tributaries in the segment beyond, therefore, resulting in a decrease in the linear shadows normally cast on the roentgenogram.[12]

D. Contour Radiolucencies Bordering the Thoracic Wall, Mediastinum and Diaphragm

Bordering the thoracic wall	Gas-fluid pockets
Pneumothorax and hydropneumothorax	Abscess
Spontaneous	Hydropneumothorax
Inflammatory	Congenital cysts
Induced	Bordering the diaphragm
Bronchopleural fistula	Paralysis of the left diaphragm
Traumatic	Eventration left diaphragm
Bordering the mediastinum	Diaphragmatic hernias (hollow viscus)
Mediastinal emphysema	Pneumoperitoneum
Lung "herniation"	Subphrenic abscess
Herniation of viscus (hollow)	

1. Thoracic wall: Introduction of air into the potential pleural space results in a peripheral zone of radiolucency without lung markings, bounded by the chest wall or mediastinal surface and the fine curvilinear density of the visceral pleura of the partially collapsed lung. Air may enter the pleural space as a result of conditions which may or may not be evident on the roentgenogram. Very minor degrees of pneumothorax are frequently overlooked and are best demonstrated with expiratory films. If the pneumothorax is extensive and of the tension type (ball-valve mechanism) there is not only an increase in radiolucency of the hemithorax with lack of pulmonary markings, but also depression of the ipsilateral leaf of the diaphragm, compression atelectasis of the underlying lung and even possibly a mediastinal shift to the contralateral side. Fluid may initially be present with pneumothorax or may appear later depending on the type of underlying lesion. Synechia of the pleura may also be present initially or may develop subsequently. The presence of these adhesive bands leads to localized areas of radiolucency

which in combination with fluid and underlying lung disease produces bizarre distortions of the lung, mediastinum or diaphragm. The resulting loss of the normal landmarks makes the evaluation of the roentgen findings more difficult. Pneumothorax or hydropneumothorax trapped in unusual locations may at times be difficult or impossible to differentiate from intrapulmonary conditions, as pneumatoceles, "vanishing lung" cavity, or extrapulmonary conditions as diaphragmatic herniation of a hollow viscus.

2. Mediastinum: (1) Mediastinal emphysema is characterized by a radiolucent band bounded by the mediastinal pleura on one side and by the mediastinal structures on the other side. (2) Lung "herniations" usually occur anterior to the heart with displacement or protrusion of the pleura across the midline by the ballooned lung into the opposite hemithorax, less commonly across the midline in the retrocardiac region, and rarely across the posterior part of the upper mediastinum. Radiographically it appears as a curvilinear density with the convexity toward the opposite hemithorax. (3) The problem of herniation of a hollow viscus, as mentioned before, is usually resolved by barium studies. (4) Gas-fluid pockets caused by congenital cysts, mediastinal hydropneumothorax and mediastinal abscesses may be very difficult or impossible to differentiate from each other radiographically.

3. Diaphragm: Paralysis of the left leaf of the diaphragm, eventration with gaseous distention of a hollow viscus beneath and diaphragmatic hernia of a hollow viscus at times simulate other radiolucent intrathoracic lesions. Barium studies are frequently necessary to differentiate these.

CONCLUSIONS

Despite the lack of specificity of roentgen signs, roentgenology of the chest is a most important method of recording and evaluating organic intrathoracic lesions. The present lack of specificity will be reduced to a minimum only after a sufficient number of controlled cases, complete with clinical, laboratory and pathologic data, are made available for proper statistical analysis. In the meantime the drawbacks resulting from the lack of specificity can be reduced by making greater use of the best available roentgen methods.

Acknowledgment: For the preparation of illustrations the authors are indebted to Miss Shirley Baty.

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Fluoroscopy of the Chest

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WHILE fluoroscopy as a series of fleeting glimpses should rarely be considered sufficient in itself to establish a diagnosis, it does provide a valuable and often necessary preliminary to the more leisurely and detailed film examination, particularly when such a complex mass of moving parts as the chest is involved. Its main advantages over filming are observation of motion (i.e., active physiology), and the most advantageous positioning of the patient for subsequent roentgenograms. This article will deal with examinational procedures in chest fluoroscopy and the fluoroscopic differential diagnosis of various commonly encountered chest conditions.

THE EXAMINATION

In preparation for examination the patient is placed behind the fluoroscopic screen, facing the examiner, with the x-ray tube behind him. His chest touches the screen to avoid excessive magnification and hence distortion. The patient is stripped to the waist, but may wear a light weight gown.

The physician's main preparation is accommodating his eyes to the situation. The subject of dark adaptation has been dealt with in detail elsewhere.[1] Suffice it to say here that the examiner's eyes are ready when he can see the medium-sized pulmonary vessels as a fine, reticulated pattern adjacent to the hilar shadows. This pattern will appear most prominent in the middle lung field, gradually fading out and disappearing as the vessels approach the lung peripheries. In this connection it should be mentioned that the day is already present when with the use of apparatus employing image intensification, more accurate fluoroscopy can be performed even though no attempt be made at previous dark adaptation. This special apparatus is not yet in general use because of expense and the large amount of space necessary.

The fluoroscopist's examination will be most rewarding if a definite plan is followed: (1) general survey of the chest, (2) positioning and localization, (3) detailed survey and (4) observation of diaphragmatic and mediastinal movements.

General Survey. The first rapid survey is with wide open shutters, the entire chest being visible. The butterfly-shaped hilar shadows are noted as landmarks, the patient's left hilus normally being a little higher than the right. Conversely, the left diaphragm will normally appear somewhat lower than the right (which is pushed upward by the liver to about the level of the sixth rib anteriorly).

Under normal circumstances both lung fields will be equally illuminated, and the reticulated pattern of the branching pulmonary artery, as noted, will appear prominent in the inner third of each lung field, fading out toward the peripheries.

The mediastinal shadow presents a problem in anatomy, for it is composed of a number of structures, the normal shape of which must be familiar to the examiner if abnormality is to be detected.

Ordinarily, this first rapid gross survey will not reveal abnormal opacities, but since the examiner must pass judgment on the shadows he does see, he must be aware of the criteria for a visible lesion, and the normal shadows which may be confused with abnormality.

The Visible Lesion. It must be (1) large enough, (2) dense enough and (3) viewed from the most advantageous angle.

1. Usually, unless the lesion is at least about ½ inch in its greatest diameter, it cannot be seen fluoroscopically.

2. The lesion may have grown considerably larger than ½ inch but still not be visible because it is not dense enough to cast a definite shadow, as sometimes occurs in pneumonia, early tuberculosis or neoplastic metastasis (although the x-ray film may show up the disease in such instances).

3. The problem discussed here is of a shadow with such a density so that in one view its margins fade out gradually, whereas in another view its margins end abruptly. A spindle-

shaped shadow is one type in mind. In one projection the fading margins are present, in the other it is only seen as a circle. When such a lesion is present in the lung parenchyma, physiologically, the eye finds it more difficult to see when so viewed that its margin is not sharp but fades out. It becomes easier to see as the patient is rotated and an appearance of a solid ball is projected so that the distinction between normal and abnormal is sharp and abrupt.

Confusing Normal Shadows. The *nipple* is seen as a nodular shadow above the faint haze cast by the base of the breast. Because of possible confusion with a nodular type lesion, the examiner must confirm the presence of nipple. If the breast is moved and the nodular shadow moves with it, the shadow is the nipple; if it does not so move, it is not the nipple and calls for further investigation. The *vertebral borders of the scapula* must be recognized as such if they are not to be confused with lobar consolidations. *Overlying neck muscles* may shadow the apices of the lungs; manipulation of these muscles by hand should clear up the field, although special apical roentgenograms must be resorted to occasionally. *An opacity in the base of the neck* may appear either on the film or fluoroscopically to be present in the lung apex. Again, to clear the dilemma, the patient is placed behind the screen, and after locating the questionable shadow the examiner attempts to grasp it with his fingers. If he can then manipulate it so that movement of the questionable shadow is visible on the screen, the presence of the lesion in the neck (rather than lung apex) is confirmed. *Chondral cartilage calcifications* are sometimes seen as multiple shadows. Fluoroscopic confirmation comes from viewing their movement with the ribs on respiration. *Widening of the mediastinal shadow* may be due, among other things, to scoliosis of the dorsal spine. To prove the widening is due to the spinal shadow, the examiner fixes his gaze on the questionable portion of the mediastinal shadow and rotates the patient to either side. A *spinal* shadow becomes obvious with this maneuver.

Positioning and Localization. If a suspect opacity has been noted on the general survey, positioning must be done before detailed examination can take place. This is simply to say that the most advantageous position for viewing the abnormality is determined so that roentgenograms may be taken from the same position, providing a more clear-cut, permanent record for detailed study.

Exact localization of the lesion can, of course, be determined by taking a number of x-ray films, but the fluoroscope can often accomplish the same end with relatively greater speed. The lesion has been seen in two dimensions: length and breadth; now it must be pin-pointed in terms of depth. Is it in the anterior or the posterior lung field? Several methods may be used.

First, if an object (lesion) is placed between a source of light (tube) and a surface upon which its shadow can be cast (screen), the shadow will be larger and hazier the farther the object is from the shadow surface; conversely, a smaller and more distinct shadow will result the closer the object is to the shadow surface. Fluoroscopically applied, if the abnormal opacity appears smaller and more sharply demarcated when the patient faces the examiner than when he is turned with his back to the screen, the lesion may be assumed to be in the anterior field. The reverse situation indicates posterior localization. (Fig. 1.)

Secondly, one may picture a circle, such as a clock face laid flat; 12 o'clock represents the posterior field, 6 o'clock the anterior. If this circle (representing the patient) is rotated in clockwise fashion, an object (lesion) in the "12" area will move from left to right—in the same direction as does the spine; an object in the "6" (anterior) area will move from right to left. (Fig. 2.)

Fluoroscopically, this "law of the circle" not only establishes anterior or posterior field but also can be carried a step further to approximate a lesion's depth within the field. An object on the periphery of a moving circle will travel more rapidly than an object closer to the center. Thus an opacity which moves with about the same speed as the rotated patient will advise the fluoroscopist of a peripherally located lesion, while a slow moving lesion should be deep seated.

Finally, normal thoracic movement may be put to diagnostic use. It will be important to determine whether a lesion adjacent to a rib is free or attached to the rib. During inspiration the ribs move upward and the diaphragm descends, the expanding lungs following this descent. Hence if the lesion follows the downward movement of the lung on inspiration, it is

within the lung; if it moves upward, following the ribs, it should be adherent to the rib.

Detailed Survey. If the first general examination yielded negative results, a detailed survey follows immediately. Even if a lesion is discovered and localization and positioning takes place, a more intimate scrutiny will now be necessary.

The shutters are narrowed to increase contrast, and, starting with the lung apices, the screen is moved down section-by-section, examination of each area including a com-

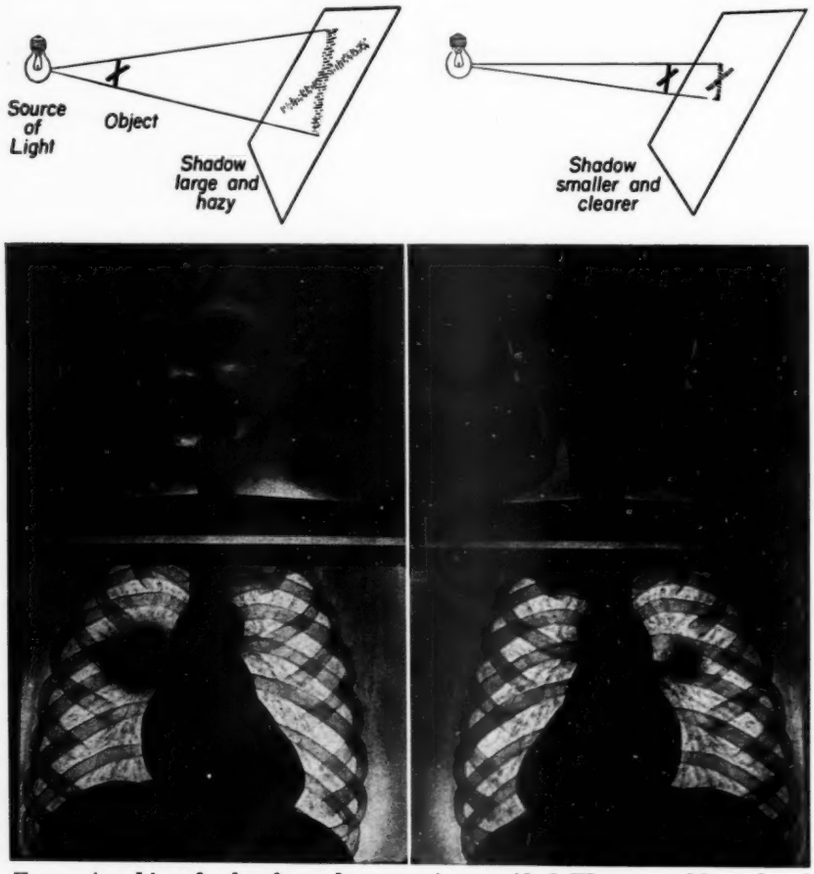

FIG. 1. An object farther from the screen is magnified. The same object placed closer to the screen is smaller and sharper. The lesion in the chest is thus placed posteriorly.

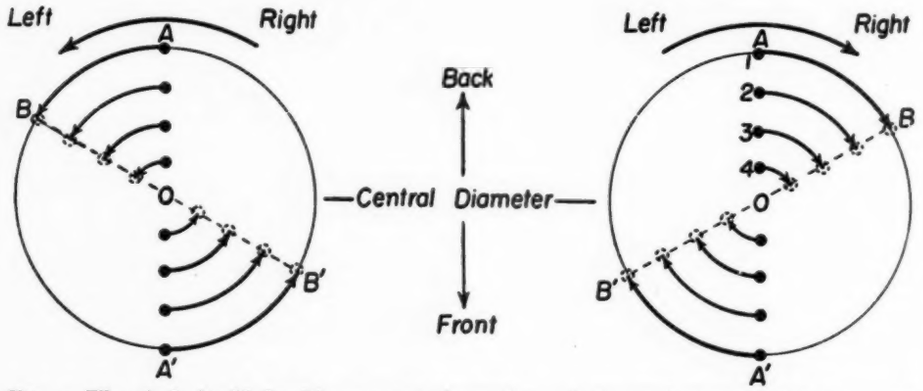

FIG. 2. The circle itself should represent the patient: A the patient and A′ the sternum. All structures in the posterior half of the chest rotate in the same direction as A. Structures anteriorly rotate with A′.

parison of left and right sides. Deep inspiration will show air entry by increased illumination; sometimes the patient is requested to cough for this purpose. The supraclavicular areas, subclavicular, the mid-lung fields and lung bases are studied for abnormalities in this fashion.

At the base of the lungs the diaphragms are now observed, and it should be noted that certain variations in contour are normal. (It has already been mentioned that the right diaphragm is normally higher than the left.) Furthermore a sharp indentation in the normally smooth curve of the right hemidiaphragm (Fig. 3) may be caused simply by a fibrotic band, while under other circumstances the left hemidiaphragm—normally low—may be raised by the stomach air bubble or by splenic flexure of the colon. The stomach air bubble is recognized fluoroscopically by its round contour and absence of inner haustral markings, splenic flexure by haustral markings within air-distended loops. Both conditions must be distinguished from eventration of the diaphragm which will be discussed later.

As a matter of fact, the careful examiner will always observe the subdiaphragmatic area, particularly studying the stomach air bubble. (Fig. 4.) Normally the magenblase is thin-walled when filled with air, fitting snugly beneath the diaphragmatic cusp. If, however, with the patient in upright position space of any great extent appears between the stomach top and left hemidiaphragm, a pathologic disorder should be suspected. A typically ragged invasion of the rounded air bubble may mean carcinoma of the cardia of the stomach. Again, however, normal shadows must be considered; one must rule out the distorting effect of thickened mucous membrane of the stomach and impingement of the liver, heart, splenic flexure and, in some individuals, the spleen. Ordinarily a pear-shaped magenblase means normal secretion, while a spherical air bubble with fluid level (especially in a fasting patient) indicates hypersecretion.

Some Special Examinational Problems. Determining fluid levels: Since fluid levels may show up fluoroscopically in any part of the chest, it is imperative that the examiner be able to ascertain with certainty whether the questionable shadow line actually is fluid or represents a density of some other nature. The procedure is simple. A glass partly filled with water will show a horizontal line, representing

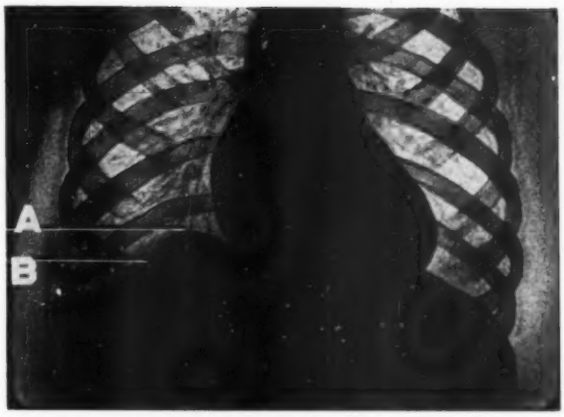

FIG. 3. Sharp indentation (B) found in the right diaphragm, producing cusp (A); this is a normal variant.

the fluid level, parallel to the floor. No matter how the glass is tilted, the fluid level will remain parallel to the floor. On the contrary, a non-fluid horizontal line on the glass itself (e.g., a dried ring left by a previous fluid) will tilt when the glass is tilted. The same principle applies fluoroscopically. If a shadow is seen on the chest, with a horizontal straight edge at top which gives rise to suspicion of fluid (as seen in pleural effusion or in an abscess cavity), the patient should be tilted in various directions and the effect of such tilting on the suspect shadow line observed. (Fig. 5.)

With the patient in the frontal position, this method will not always give satisfactory results. Observation laterally may discover a fluid level not otherwise seen (as, for example, in the posterior costophrenic sinus). At times the findings will be more clearly made if the rays are used horizontally with the patient in a supine position.

Infiltrations or lymph nodes versus blood vessels: On occasion it will be important to determine the appearance of the blood vessels, as in atelectasis. To distinguish between blood vessels and lymph nodes or hilar glands, the Valsalva maneuver can be put to advantage. With intra-alveolar pressure thus increased, the pulmonary vessels are compressed, with consequent decreased degree of filling, and on the fluoroscopic screen the radiating pattern of these vessels becomes thinner and less pronounced.[2] Lymph nodes and hilar glands, on the contrary, are not affected in this fashion by such increase in pressure, largely retaining their size, shape and prominence, and thus the distinction is made. Additionally, with the

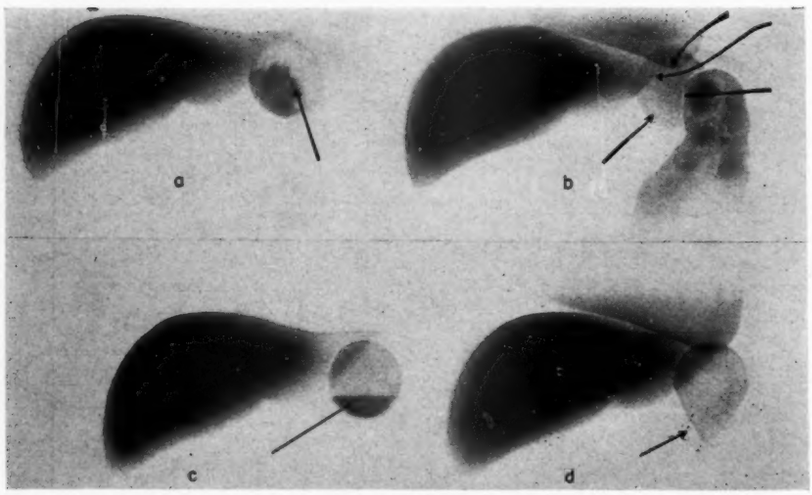

FIG. 4. (*a*) Carcinoma of the stomach; (*b*) fundus deformed normally by liver, splenic flexure, heart; (*c*) hypersecretion as evidenced by fluid level in fasting stomach; (*d*) normal pear-shaped stomach.

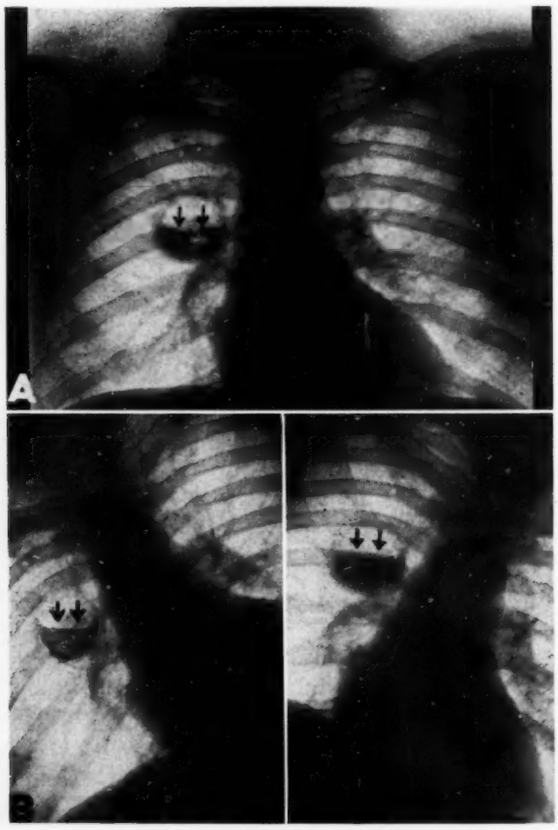

FIG. 5. A, shadow in right lung field to be "tested" for fluid level. B, patient leaning toward right and left reveals horizontal shadow remaining parallel to floor, thereby confirming presence of fluid level.

Valsalva maneuver the narrowing and fading out of hilar vessels frequently reveals large glands formerly covered and hidden.

To further distinguish blood vessels from lymph nodes, rotation can be used. If the patient is turned, a blood vessel shadow may elongate or disappear, whereas little or no change in shape will be noted with lymph nodes or glands.

Pseudocavity: This is in effect a normal shadow which may be confused with a disorder, but its occurrence is common enough both fluoroscopically and on the x-ray film that it warrants special mention. Fortuitous combinations of overlapping shadows of normal blood vessels sometimes produce the appearance of a cavity. The distinction between "real" and "apparent" is easily made by rotating the patient behind the fluoroscopic screen. A true cavity will move and continue to be seen as the patient rotates, while a pseudocavity due to blood vessel overlap will quickly disappear.

Observation of Diaphragmatic and Mediastinal Movements. Closely allied with the detailed survey, this part of the fluoroscopic examination is of paramount importance for the chest physician or surgeon, for actual function or the lack of it can be seen and this is often important in making a diagnosis.

Diaphragmatic movements: We have already noted how the up-and-down diaphragmatic movements during respiration can be visualized fluoroscopically. Lack of such movement, however, is sometimes difficult to detect because the moving rib shadows create the optical illusion of diaphragmatic movement. The degree of movement, if there is movement at all, can be determined by the following simple

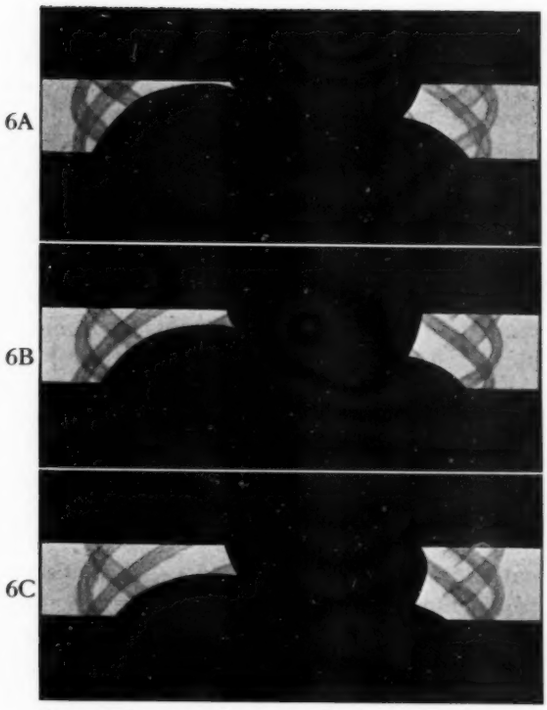

FIG. 6. A, space between diaphragm and upper shutter smaller (expiration); B, space between diaphragm and upper shutter large (inspiration); C, space between diaphragm and upper shutter neutral position.

procedure. The shutters are narrowed so that only the diaphragmatic cusp shadows and a small illuminated area of lung above them are seen. This space (aerated lung) is watched, *not* the diaphragms. When the patient inspires, the space should become larger as the lung fills with air and pushes the diaphragms down; on expiration, the space should become smaller (the diaphragms rising). (Fig. 6.) With experience, the observer can determine whether the movements are normal, increased or decreased. If the space does not change with respiration, there is no diaphragmatic movement (paralysis).

(An even simpler method is to provide a stationary landmark as a point of reference by the examiner placing his finger on the screen atop the diaphragmatic shadow; one need only observe whether the shadow moves away from the fingertip on respiration—and how much, or whether it remains stationary.)

Lack of movement, however, may not be pathologic. Some individuals customarily breathe without diaphragmatic excursions; if asked to sniff, however they will show a short, jerky movement of the diaphragm, which rules out paralysis.

Diminished diaphragmatic movements: While increased movements, as a persistent flutter, may accompany epidemic encephalitis, influenza and cardiospasm associated with hypocalcemia, decreased diaphragmatic movements are usually of more specific diagnostic value. The decrease may be on either or both sides. It may be of subdiaphragmatic or intrathoracic origin (an important point in pneumonia). The ultimate in decreased movement is, of course, paralysis.

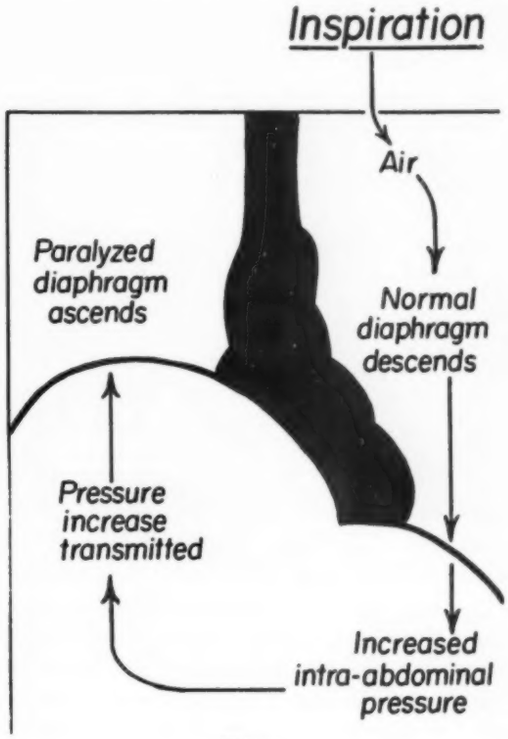

Fig. 7.

A paralyzed diaphragm can be diagnosed by the previously mentioned methods, including the "sniff test," and the examiner should also be aware of so-called paradoxic movements (Kienbock's phenomenon) which is indicative of one-sided paralysis. (Fig. 7.) On inspiration the normal hemidiaphragm will descend in normal fashion, while the abnormal side will simultaneously rise because the increased intra-abdominal pressure is transmitted to the paralyzed hemidiaphragm, pushing it upward. On expiration the mechanism works in reverse. This phenomenon is noted occasionally in atelectasis and in some inflammatory lung

lesions. With correction of the condition, the paralysis disappears.

Diaphragmatic paralysis has particular diagnostic value in lung cancer. Carcinoma of the lung frequently spreads metastatically to involve the phrenic nerve and, since the phrenic nerve exercises control over diaphragmatic movement, diaphragmatic rise and paralysis ensues. Opinion on the operability of such cases is divided, but the important point for the examiner is that if a patient with cancer of the lung is fluoroscoped and the diaphragm in question is seen high and presents evidence of paralysis (Kienbock's phenomenon), phrenic nerve involvement must be suspected.

Paralysis of the phrenic nerve has been said to be the cause for eventration of the diaphragm. The nerve paralysis may be only partial and diaphragmatic movements may or may not be present in such case; but the involved didphragm will be raised high. Since the condition usually occurs on the left side, it may be confused with simple raising of a normal diaphragm by bowel or gastric air distention. (The left diaphragm lies directly against the intestine and can be pushed up thus by gas, but the right diaphragm will not be seen to rise from such cause since the liver intervenes.) The differential diagnosis can usually be made by watching for diaphragmatic movement. The eventrated diaphragm presents evidence of paralysis (Kienbock's phenomenon).

Mediastinal movements: These movements are of obvious value in examination of the heart, but since the latter could well be a monograph in itself and has been described in essentials elsewhere,[1] we shall confine ourselves to a brief discussion of mediastinal movements associated with pulmonary disease.

Significant changes in mediastinal movement are sideways. These shifts, sometimes easy, sometimes hard to detect, are observed by a technic similar to that used in examining for the up-and-down movements of the diaphragm. The fluoroscopic shutters are narrowed so that the examiner sees only the mediastinal shadow, with a long, narrow segment of illuminated lung on either side. On inspiration, these segments of aerated lung should become larger, the mediastinal shadow contracting. This contraction is normally bilaterally equal, i.e., the mediastinum should not be displaced toward one or the other side. If on inspiration the visualized lung segment on the left enlarges and the segment on the right decreases, the mediastinum is shifting to the right (or vice versa). The shift may also occur on expiration. In either instance a pathologic condition is indicated. Having the patient take short, deep breaths will exaggerate the movement.

On *inspiration*, mediastinal shift toward one lung means that that lung has decreased intrathoracic pressure (i.e., it is not receiving the full complement of air that the other side is getting). This occurs, for example, in bronchostenosis of one side and in marked bullous emphysema, where blockage of the smaller bronchi obstructs free entry of air. On *expiration*, mediastinal shift away from one lung indicates some such condition as emphysema with a ball-valve type of obstruction which does not allow normal egress of air (i.e., the affected lung is retaining more air than the normal lung). In all instances pathologic mediastinal movement is *away from* the lung with greater intrathoracic pressure (showing as enlarged illuminated lung area on the fluoroscopic screen), *toward* the lung with less pressure (showing as decreased, less illuminated lung area on the screen).

Fluoroscopic study to determine if a mediastinal mass is pulsating is somewhat more difficult and demands experience. The shutters are narrowed down on the abnormal shadow to avoid secondary radiation. The difference between expansile and transmitted pulsation can only rarely be seen fluoroscopically.

Examination of the mediastinum should also include study of the esophagus. Detailed study[1] of the subject is beyond the scope of this article, however, and we can only say here that the examiner must be familiar with the normal course of the tract, normal variations and impinging structures before he can hope to understand pathologic manifestations on the fluoroscopic screen.

SPECIFIC PATHOLOGY

Fluoroscopic observation of certain pathologic conditions in the chest has been discussed in connection with various maneuvers and phases of the examination. Following is a brief exposition of how the examiner may specifically investigate some of the more commonly encountered disease processes in the chest by the use of fluoroscopy.

Tracheal Deviations. The trachea, like the esophagus, should be examined as part of the

chest survey and, again, the normal course and variations should be familiar to the examiner. An example of normal deviation which may be confused with a disorder is the slight deviation to the right (with the patient in the frontal position) as the trachea passes behind and to the right of the aortic arch. Pathologic angulation must be distinguished from such normal variations; substernal thyroid is often implicated, and the diagnosis must be confirmed by further study.

Fluoroscopic examination will also give clues to the firmness and resistive powers of the trachea.[3] The Valsalva maneuver is utilized to this end (or, alternatively, having the patient cough). With intratracheal pressure increased in this fashion, tracheomalacia will be visualized by wide dilation of the previously narrowed segment. Conversely, the Muller experiment on expiration (or asking the patient to sniff) will demonstrate softening of the tracheal wall by marked narrowing of the involved area. In either instance the malacia may be one-sided and visualized as eccentric. In any event conclusive evidence of softening of the tracheal rings is a serious prognostic sign of possible tracheal collapse and sudden death, and in such case fluoroscopic findings give a clear indication for operation. Substernal thyroid may be implicated, or long-existing goiter or mediastinal tumor.

Substernal Thyroid. Substernal thyroid manifests itself fluoroscopically as a mass in the upper mediastinum, adjacent to and very likely angulating the trachea. Other conditions can produce the same appearance, so that confirmation is needed. Tracheomalacia as a concomitant finding (noted previously) gives some degree of additional evidence. To clarify the diagnosis further, the patient is asked to swallow. If the suspect shadow rises with the swallow, then falls back, the observer can assume that the mass is adherent to the trachea. (Fig. 8.) Substernal thyroid is the most common condition showing these features.

One important point should be mentioned in connection with the swallowing maneuver. The physician may experience difficulty in seeing the abnormal shadow rise on deglutition. This may be laid in large part to the expectation of seeing a very pronounced movement, whereas in reality the rise is small. One can test this by placing his finger on the larynx and swallowing; the rise is perhaps no more than ¼ inch, even though it can be felt quite distinctly. The same "finger test" as mentioned earlier, then, can be used here. The examiner's finger (as a stationary point of reference) is placed on the screen at the inferior border of the shadow in question. The patient swallows. If the shadow moves up and away from the finger, no matter how small, the movement should be clearly seen, and the diagnosis of adherent mass is made.

FIG. 8. Mass deforming trachea and rising with deglutition is apt to be substernal thyroid.

Subdiapbragmatic Abscess versus Primary Intratboracic Pneumonia. A common radiographic finding in postoperative patients is a pneumonic process in the lower lungs. Here the joint radiographic-fluoroscopic study can determine with considerable accuracy whether the involved lung area suffers lymphatic extension from a subdiaphragmatic abscess or whether a pneumonia of intrathoracic origin is present. The following points give clues: (1) In subdiaphragmatic abscess, diaphragmatic movements become restricted at an early date, with the diaphragm eventually raised and fixed. Although decreased movements also occur (but not always, and to a less obvious extent) in primary intrathoracic pneumonia, rarely does the diaphragm become as rigidly fixed. (2) In subdiaphragmatic abscess, the

pneumonic process is visualized as closely adhering to the diaphragmatic outline. In a primary pneumonia the pathologic shadow is not so closely confined to the diaphragm, greater hilar involvement is noted on the pneumonic side and some aerated lung may be

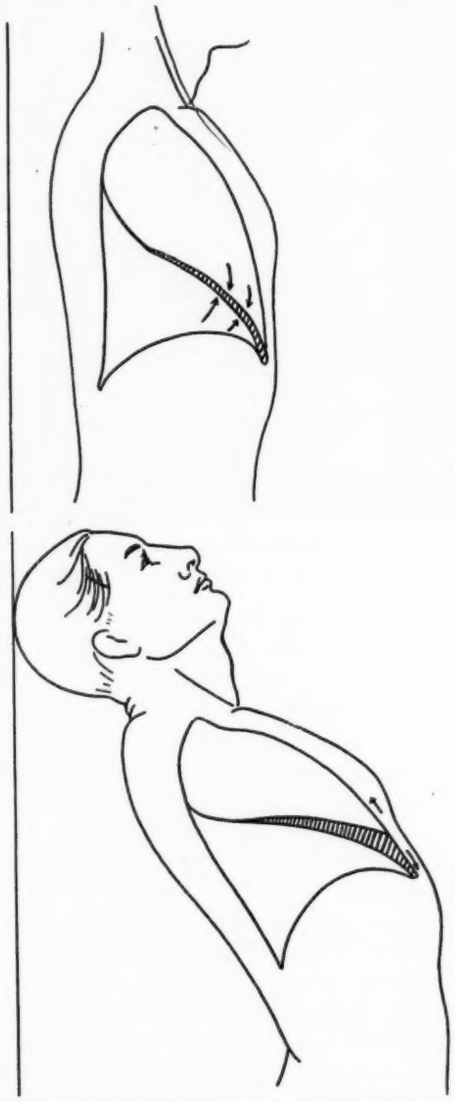

FIG. 9. Patient in conventional position; the atelectatic middle lobe is obscured. Patient in lordotic position; the atelectatic middle lobe becomes obvious.

present between the lesion and the diaphragm. (3) Subdiaphragmatic abscess produces a pneumonia that extends through the pleural lymphatics to the lung; hence, pleural effusion with obliteration of the costophrenic sinus on the diseased side often occurs—a sign less commonly observed with primary intrathoracic pneumonia. (4) Accumulation of air and a fluid level below the diaphragm will be observed in something like 25 per cent of subdiaphragmatic abscesses. This must be differentiated from subdiaphragmatic air space without fluid level occurring in laparotomy patients.[5] Most subdiaphragmatic abscesses occur on the right side. The distance between the upper edge of the cusp and the bottom of the liver shadow is normally about 20 cm. If this distance increases, a subdiaphragmatic abscess must be suspected of pushing the liver down. Obviously this finding must be assessed in relation to other findings; the liver may be enlarged, or some other structure may be displacing the liver downward.

Atelectasis. The fluoroscope offers the opportunity for certain specific observations in diagnosing this condition. The pulmonary arteries, as shadows radiating out from the hila, on inspiration normally fan out and greatly separate. When a lung is partially collapsed, this fanning out is not seen. On expiration the fanned out vessels should come together again, but in an atelectatic area this does not occur. Abnormal lack of the normal fanning movement can be more clearly seen by comparison with the changing pattern in the uninvolved lung areas.

Atelectasis of the right middle lobe, particularly, may not be seen when the patient is in the frontal position because the upper lobe overlaps it anteriorly, the lower lobe posteriorly. Moreover, compensatory emphysema of the upper and lower lobes will cause hyperillumination (because of increased alveolar distention), canceling out the atelectatic effect in the middle (which ordinarily would be one of opaque shadow, caused by air paucity); this mixture of hyperillumination and diminished illumination produces the illusion of normal lung. However, if the patient steps forward 6 inches and leans back so that the back of the head touches the back panel (lordotic position), the upper lung separates from the lower lung, allowing the middle lobe and its shadow of atelectasis to be visualized. The lordotic position has an additional advantage here in that the middle lobe is so thrust out that the x-rays pass through more thicknesses (i.e., a greater density) of atelectatic tissue, thus making the abnormal shadow more distinct. (Fig. 9.)

In atelectasis as well as emphysema when air cannot freely move in and out of the lung

area, the blood vessel shadows cannot spread or fan together in normal fashion; rather, on respiration they will closely follow the rise and fall of the diaphragm. We can say then that whenever the middle lobe is obstructed, and the short fissure is fluoroscopically visible, this short fissure will move up and down with the diaphragm.

Emphysema. The lack of normal fanning motion of the blood vessel pattern during respiration, as seen in atelectasis, is a phenomenon also occurring in any disease process which causes obstructive emphysema (e.g., bronchial tumor), so that this sign alone is not sufficient. The actual atelectatic shadow as an increased density must be seen before the diagnosis is fully established. In emphysema the involved area will show as increased illumination or diminished density.

Pneumothorax. A clear space visualized between lung and ribs shows the presence of air and thus establishes the diagnosis of pneumothorax. This space may often be seen fluoroscopically with the patient facing the examiner, in which event the diagnosis should be confirmed with filming.

The question of positioning is of considerable importance in diagnosing pneumothorax, particularly when it is incomplete, since examination with the conventional frontal position may fail to turn up a small pocket of air between the lung and chest wall hidden by overlapping normal lung (i.e., a pocket situated *posteriorly* with normal lung in front). Rotating the patient is, of course, the answer to this problem. Even then a very small pocket of air will be difficult to see. Fortunately a simple procedure will be of quite definite aid in such instances. The patient is asked to exhale. The lung becomes smaller making the pocket appear relatively greater in size and easier to see. Here again rotation of the patient during exhalation is important.

An important point in diagnosing pneumothorax has already been made. If there is mediastinal shift on respiration, it is toward the side where intrathoracic pressure is lower; if there is fixed displacement rather than simply shift on respiration, again the displacement is toward the side with decreased pressure.

An additional sign is the peculiar heart flutter associated with the condition, and which has to do with air reaching the mediastinal surface. It can be observed fluoroscopically.

Pleural Effusion. Fluid collection in the chest when present in sufficient amounts may be seen in the frontal examination of the patient. When present in small amounts, the fluid will collect in the trough or lowest part of the chart, i.e., the posterior costophrenic angle. With the patient in the conventional frontal position, the dome of the diaphragm obscures its presence. Various maneuvers are useful in demonstrating this small amount of fluid hidden in the posterior recess. The patient may be asked to lie down in the supine position and unless loculated by adhesions, the fluid may be expected to flow upward—producing an opaque shadow in the involved hemithorax—previously clear when the patient was upright. Turning the patient into oblique positions, while he is supine is also helpful. In the erect position, turning the patient into a true lateral position also may demonstrate the fluid—by opacification of the posterior costophrenic angle.

The tube may also be raised, and the patient turned with his back to the screen, so that the deep posterior costophrenic sinus may be viewed without being obscured by the dome of the diaphragm. The image is thus projected downward on the screen; and if significant findings are noted, roentgenograms can be taken in the same fashion.

This method can likewise be used to view lung parenchyma deep down behind the diaphragmatic dome and not usually visualized on frontal examination: Moreover the principle can be varied to meet the needs of the situation, e.g., with the patient in the frontal position the tube can be *lowered* to project apical lesions above the clavicle.

Pulmonary Fibrosis. General multifocal fibroid reactions within the lungs have been ascribed to tuberculosis, bronchiectasis, syphilis, radiation therapy, asthma, pneumoconiosis and scleroderma.[5] Whatever the etiology, fluoroscopy can at least establish the presence of such processes through the observation of typical movements. With normal respiration diaphragmatic rise with expiration is slower (so-called lag) than the descent on inspiration. In pulmonary fibrosis this lag is accentuated; in exaggerated cases, indeed, diaphragmatic paralysis may occur.

With pulmonary fibrosis certain mediastinal and tracheal clues are obtainable. The mediastinum, paradoxically, appears wider with

inspiration, narrower with expiration. Widening of the tracheal air space may occur and is diagnostically significant.

SUMMARY AND CONCLUSIONS

The writer would add but three brief concluding remarks. First, the examination will be worthless if the examiner's eyes are not properly accommodated to the examination milieu. The fluoroscopic image is so rapid, the shadows so often far from clear-cut, the mass of complex detail in this situation such a problem in separating the diagnostic wheat from the chaff, that the eyes must operate *physiologically* at an optimum level.

Secondly, the fluoroscope is a potentially dangerous instrument not only to the patient and the examiner, but also to attendant nurses and students. The necessary precautions should be known and observed. The widespread use of the machine makes this rather obvious point worth emphasizing.

Finally, diagnostic proficiency comes only with considerable practice. The examiner will profit from taking advantage of every examination performed and carrying it out properly. As in any field of medicine, experience and acquaintance with the normal will prove invaluable in recognizing the abnormal.

In summary, it has been pointed out that while fluoroscopy must usually be considered an adjunct to film examination, it does have certain advantages: (1) it is a truly *in vivo* examination, the diagnostic possibilities of seeing functioning parts in motion, normal and abnormal, being obvious; (2) the mobility of the method and the rapidity with which it can be carried out provide an opportunity to determine the most profitable angle for viewing pathologic conditions thus "setting up," as it were, the roentgenographic examination and avoiding the taking of time-consuming multiple x-ray films.

Preparation of patient and examiner has been briefly described, and a recommended plan of fluoroscopic examination of the chest presented in some detail: (1) general survey, (2) positioning and localization, (3) detailed survey and (4) observation of diaphragmatic and mediastinal movements. The criteria for visibility of lesions have been defined and solutions for some special examinational problems offered.

Short descriptions of the fluoroscpic findings in a few of the more commonly encountered chest conditions have been given, and an attempt has been made to include differential diagnostic aspects.

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Current Radiographic Technics in the Diagnosis of Pulmonary Disease

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MORE than half a century ago Roentgen's discovery of the x-ray led early observers to comment on the degree to which imagination contributed to the interpretation of physical signs in the chest. The limitations of physical examination are now better understood, but those of the conventional chest roentgenogram still need to be emphasized. These limitations are in effect indicated by the varied x-ray technics currently used in the diagnosis of chest disease. Such a variety of procedures and the fundamental differences in their principles also indicate clearly that no single method of x-ray study can serve all diagnostic purposes. This review is intended to orient the reader to a field of increasing complexity, calling attention to ordinary procedures which are often neglected, as well as those that require special equipment.

Current technics in x-ray examination of the chest might best be considered on the basis of their contribution to: (1) detection of disease, (2) differential diagnosis, (3) localization for surgical resection, (4) evaluation of therapy, (5) estimation of function. While the various technics generally serve more than one such purpose, they all tend to supplement each other.

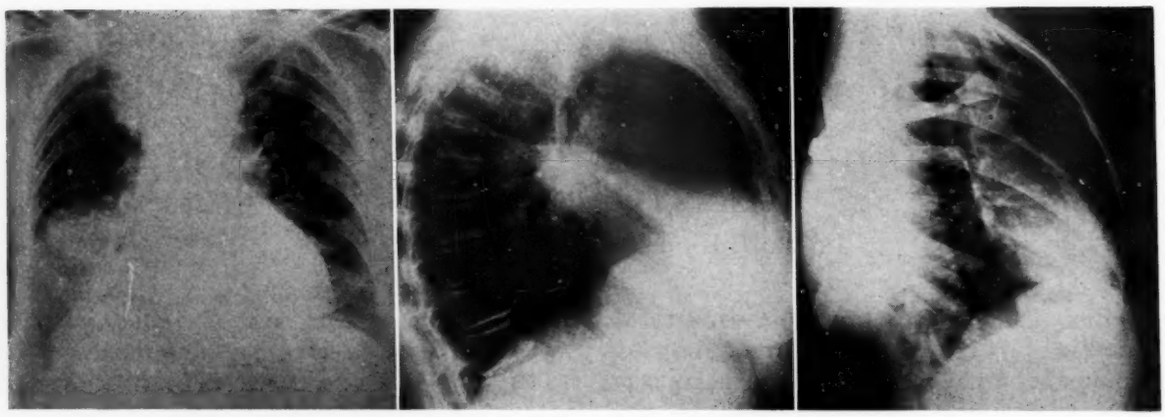
The *conventional chest x-ray* used for routine examination and for survey purposes is also referred to as a postero-anterior (p-a) x-ray. The latter designation always indicates the direction in which the x-rays travel through the body to the recording film. Properly taken such a film serves admirably for scouting purposes and through deductive interpretation yields considerable information.

A complete evaluation of the conventional x-ray and its limitations will be published elsewhere. For present purposes it must suffice to call special attention to those areas of the chest roentgenogram in which disease is frequently obscured or easily overlooked, namely, the lung apices and retroclavicular regions, the parahilar or lung root regions, the retrocardiac, anterior mediastinal and retrodiaphragmatic regions. These areas of the ordinary chest x-ray might be referred to as "danger zones," for at all times they demand the observer's most critical attention. The slightest suspicion offered by history, symptoms or physical examination warrants their special investigation.

Apart from its place in the initial detection of disease the conventional postero-anterior chest x-ray serves as a standard for following the course of a disease and its response to therapy. Its usefulness for the latter purpose will, however, depend on the extent to which it originally revealed the disease. It must also be emphasized that the disappearance of a lesion on the ordinary x-ray picture does not exclude the persistence of clinically significant disease in that lung. In other words, before or after treatment the conventional chest x-ray may and often does fail to reveal the true extent of a lung disease or the degree of its persistence. Every experienced thoracic surgeon knows this.

While it is necessary to confirm the disappearance of pulmonary lesions by special x-ray technics before abandoning therapy and to verify the extent of a disease before undertaking its resection, such confirmation does not imply the supplementary use of ordinary lateral or oblique chest x-rays. Instead, the specific technic required in each case must be determined by the nature of the original disease. These points will be clarified in the course of the further discussion.

Stereoscopic chest x-rays in any position offer one basic advantage to all observers; that of examining two pictures taken from slightly different angles. At times one of these may reveal information which is otherwise obscured by a rib or an overlying shadow. Except for this it must be recognized that stereoscopic impressions are highly subjective and dependent on a variable personal factor. Even with practice not everyone can achieve the same degree of stereoscopy. If two films are to be



1A 1B 2

FIG. 1. A, conventional chest x-ray showing rounded shadow in right lower lung associated with elevation of the anteromedial segment of the diaphragm. An unrelated large thyroid adenoma is seen extending out from the superior mediastinum on the right. B, ordinary lateral chest x-ray confirming elevation of anteromedial segment of the right diaphragm and proving the lower lung shadow to be the result of right middle lobe atelectasis.

FIG. 2. Special lateral chest x-ray. This was taken with the right side of the chest against the film, the right arm extended up alongside the head, the left arm and shoulder depressed downward and back to a maximum degree. Slight rotation further helps to project the lower shoulder away from the mediastinum.

taken in a single position, there is generally greater advantage to taking each one from a different direction, e.g., one from the back and another from the front. In the lateral position taking one film from the right and one from the left allows better definition of lesions in either lung and on either side of the mediastinum.

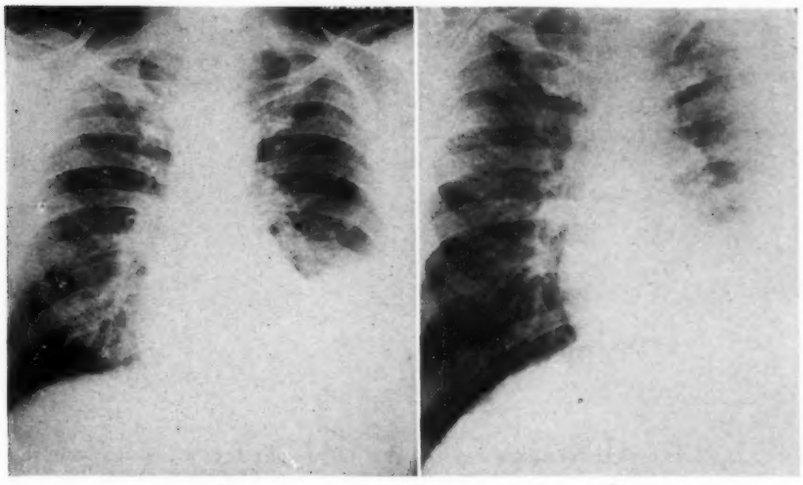
When attempting to see around a shadow such as the heart, even the oblique views will offer more advantage than stereoscopy or the slight angle of difference between its two projections. However, in dealing with such problems no generalization is implied or intended. Beyond the conventional (p-a) chest x-ray additional films should be taken only as indicated by the specific nature of the information sought.

The *ordinary lateral chest x-ray* is generally one of the most disappointing views. When requested as a routine supplement to the conventional (p-a) chest x-ray it very frequently constitutes an economic waste. This fact is not surprising if one considers that all the shadows of the opposite lung as well as those of the mediastinum are superimposed on the area being studied. It is therefore suggested that the ordinary lateral chest x-ray be used only for specific purposes such as the demonstration of interlobar fluid, of middle lobe (Fig. 1) or lingula disease, of anterior segment (upper lobe) or anterior mediastinal disease, and for the study of the barium-filled esophagus and its displacement by cardiac or mediastinal conditions.

To overcome the effect of both shoulders on the visibility of the upper mediastinum and the lung apex on either side, a *special lateral chest x-ray* can be obtained. (Fig. 2.) This is based on a variation in the position and projection of the shoulder structures, one being projected upward and the other down and back. Frequently neglected, this type of lateral chest x-ray offers a continuity in the visibility of the trachea and esophagus from the neck down into the mediastinum. The slight obliquity of the position has no significant effect on the appearance of these structures since the arc of their rotation is much less than the displacement of the peripheral structures of the thorax.

In contrast to its limitations under the conditions of conventional radiography it will be noted later that the lateral position is of paramount importance in special radiographic procedures like bronchography and planigraphy (tomography).

At this point attention should be called to an ordinary x-ray technic which is commonly referred to under a misnomer, namely, the "*lateral recumbent chest x-ray*." Taken literally such a picture would be of less value than the ordinary upright lateral view. What is actually intended by this term should be specifically



3A 3B

FIG. 3. A, conventional chest x-ray showing rounded shadow in left lower lung associated with pleural changes. B, conventional chest x-ray taken in left lateral recumbent position proves that the shadows in the lower chest are due to pleural fluid in a freely communicating space. This is evidenced by a shifting of the shadows up along the lateral chest wall and over the lung.

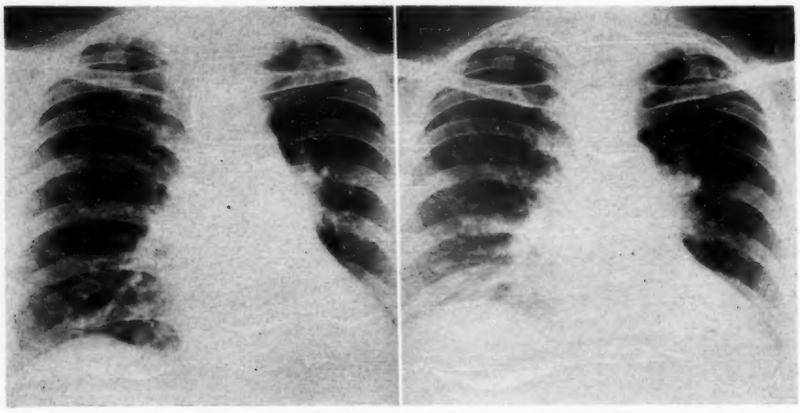
referred to as a postero-anterior (or antero-posterior) chest x-ray taken in the right or left lateral recumbent position. Too often forgotten, this simple technic helps distinguish pleural fluid from pleural thickening, provided the fluid is not loculated. (Fig. 3.) In the presence of a free pleural space the shifting of interlobar fluid with change in position helps distinguish it from parenchymal disease. Similarly, change in shape with change in position helps to differentiate cystic tumors (e.g., bronchogenic, enterogenic, pericardial) from solid tumors. Even with a diaphragmatic hernia a chest x-ray taken in the lateral recumbent position may suggest the correct diagnosis when a gastrointestinal series and a diagnostic pneumoperitoneum have failed to do so. (Fig. 9.)

Inspiration and *expiration chest x-rays* offer much of the information ordinarily gained by fluoroscopy. With such pictures the dynamic changes accompanying respiratory movements of the thorax and diaphragm can be studied leisurely and filed for future comparison.

Thus, in conjunction with the ordinary inspiration chest x-ray an expiration film may be expected to demonstrate: (1) the occurrence of mediastinal swing or rotation (Fig. 4); (2) the extent of diaphragm motion or paralysis; (3) the degree to which air is moved by each lung or the degree to which it is trapped in obstructive emphysema (Fig. 4); (4) the presence of unsuspected pneumothorax; (5) the cystic or fluid nature of a pulmonary or mediastinal condition (Fig. 5); and (6) the extent of mobility of a diaphragmatic hernia. To combine both pictures on one film through double exposure with or without a Birath-Kallquist grid sacrifices too much parenchymal information.

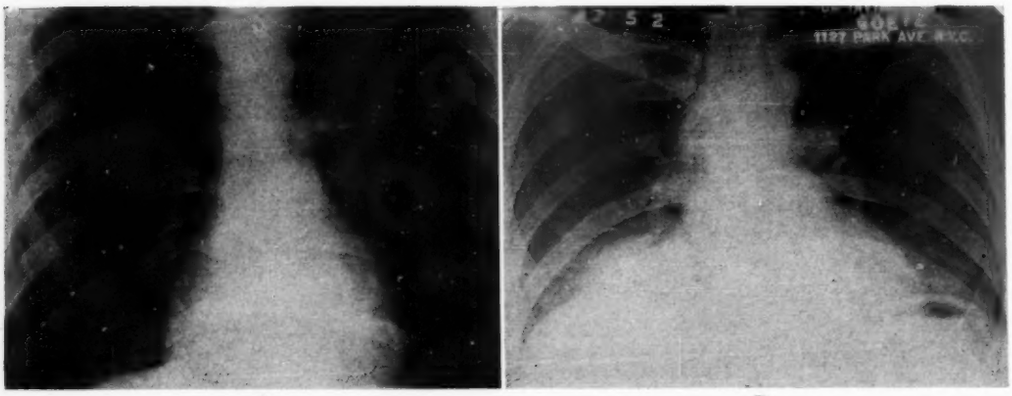
Valsalva and *Müller chest x-rays* are occasionally useful in determining the vascular nature of a pulmonary or mediastinal shadow. The Valsalva maneuver consists of forced expiration against a closed glottis, whereas the Müller maneuver consists of forced inspiration against a closed glottis. In the former instance air pressure within the thorax is increased with consequent reduction of blood volume in the right auricle, the pulmonary vessels and left side of the heart. Conversely, in the Müller test a strongly negative intrathoracic pressure or suction effect is produced with progressive overdistention of the right auricle, the pulmonary vessels and the left side of the heart. These pressure changes are classical in their effects on heart size and shape, but their influence on mediastinal and pulmonary vessels is less dramatic.

The effect of these procedures varies with the understanding and cooperation of the patient and the length of time the intrathoracic pressures are sustained before each x-ray exposure. Training the patient under fluoroscopic observation and supervision of the technic by a



4A 4B

FIG. 4. A, inspiration chest x-ray shows rotation of the heart toward the right anterior oblique position and suggests contraction of left lower lobe. Increased density of the left lung root region is also noted indicating the presence of a tumor. These observations associated with evidence of left upper lobe emphysema suggest the presence of bronchogenic carcinoma obstructing the lower lobe bronchus and stenosing the upper lobe bronchus. (This deductive interpretation was confirmed by bronchoscopy and subsequent necropsy.) B, expiration chest x-ray emphasizing the presence of obstructive emphysema in the left upper lobe. The heart is seen to rotate back toward midline as a result of the relative equalizing effect of expiration on the pull of the contracted left lower lobe. Thus the tumor in left lung root region is more clearly revealed.



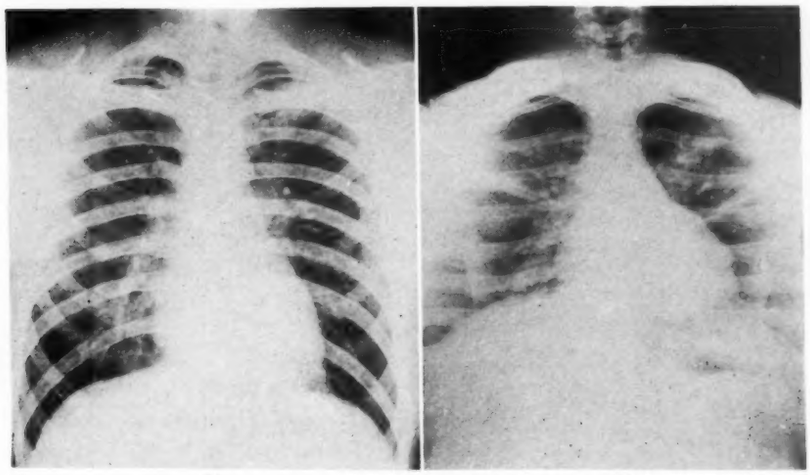
5A 5B

FIG. 5. A, inspiration chest x-ray shows a widening of the mediastinum at the base of the cardiovascular silhouette. B, expiration chest x-ray shows an expanding shadow in the cardiophrenic angle above the right diaphragm. This change in the mediastinal outline corresponding with the expiratory change in intrathoracic pressure suggested an intercommunicating cyst of the pericardium (proved surgically).

physician are therefore essential to its success. However, even with ideal cooperation the value of this procedure is limited in the presence of thromboses.

Another useful variation of the conventional roentgenogram is that referrred to as a *lordotic chest x-ray*. This depends on an altered angle of projection and is taken in the anteroposterior position with the patient standing away from the film but leaning back so that the base of his cervical spine rests on the x-ray film holder. His thoracolumbar spine is then in extreme lordosis, thus accounting for the name of this position. The proper execution of this technic requires a supple patient and a careful technician.

An alternate term, "apical-lordotic chest x-ray," is sometimes applied to the same procedure. This is less desirable since it implies unnecessary limitation to the usefulness of this position. Furthermore, it should be realized that the visibility of lesions in the anterior



6A 6B

FIG. 6. A, conventional chest x-ray showing an infiltration in the retroclavicular region on the left. B, lordotic chest x-ray showing upward projection of the clavicles with improved visibility of the underlying lesion. A cavity is also suggested just above the lung root shadows on the same side.

portion of the lung apices may actually be impaired in this position rather than improved. Conversely, lesions lower down in the chest, behind the clavicles (Fig. 6) or in front of the lung root and cardiac shadows may be projected into clearer view. As with all frontal chest roentgenograms, the scapulas must be rotated forward to either side in order not to project over the lung fields.

The *oblique chest x-rays* customarily taken in the postero-anterior position with the right or left breast against the film are referred to respectively as right or left anterior obliques. Each would correspond in general appearance to posterior oblique views taken from the opposite sides (e.g., right anterior oblique resembles left posterior oblique and so forth). The most familiar use of the oblique positions is in outlining the esophagus and cardiovascular silhouette and in estimating the size of the cardiac chambers.

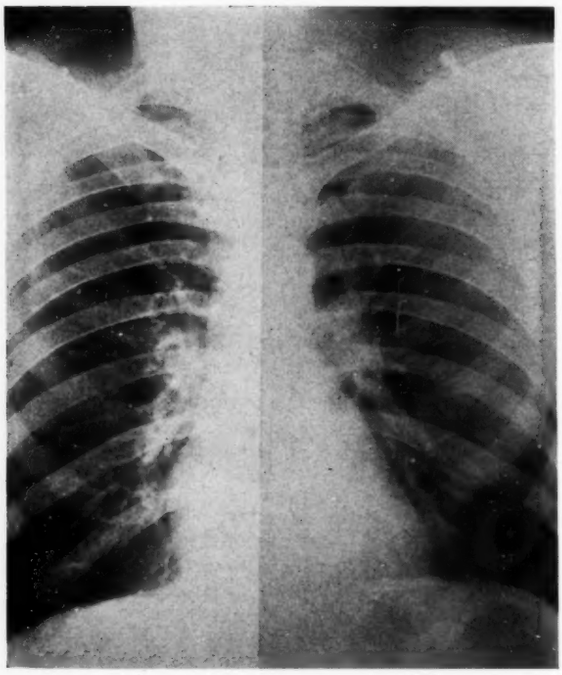
For pulmonary studies these views dissociate the lungs into four vertical quadrants consisting of anterolateral and posterolateral sectors on each side. From the right and left anterior oblique projections it is possible to obtain unopposed views of each of these vertical quadrants and to see around the cardiac silhouette.

The value of these positions in special x-ray technics will be noted later. Except for cardiac studies, the ordinary oblique chest roentgenogram is of use chiefly to those who must attempt to dissociate complex shadows without the facility for more satisfactory methods such as planigraphy (tomography).

The *grid-filtered chest x-rays* are most frequently referred to as Bucky or Potter-Bucky pictures. These pictures are obtained by interposing a lead grid between the patient and the film. The misguided technics customarily employed in obtaining so-called "Bucky chest x-rays" have usually involved unnecessary overexposure and the use of a moving grid. As a result clinicians and radiologists have frequently been discouraged from ordering grid-filtered chest x-rays.

While the thin wafer grid of the Lysholm type serves to reduce the fogging effects of secondary x-ray radiation (Fig. 7), it has virtually no effect on object-to-film distance. The increase in object-to-film distance imposed by use of the moving lead grids of the Potter-Bucky type is more objectionable in its effect on definition than is the faint visibility of lines noted with the latest type of stationary (Lysholm) grid. In spite of the excellent quality of today's ordinary chest x-ray the general use of a stationary wafer grid might be expected to lead to its further improvement.

Another important diagnostic procedure is the "*barium swallow*" or *esophagogram*. No study of the mediastinum is complete without fluoroscopic or radiographic examination of the esophagus. Whether investigating symptoms of mediastinal distress (Fig. 8A) or the possibility



7A 7B

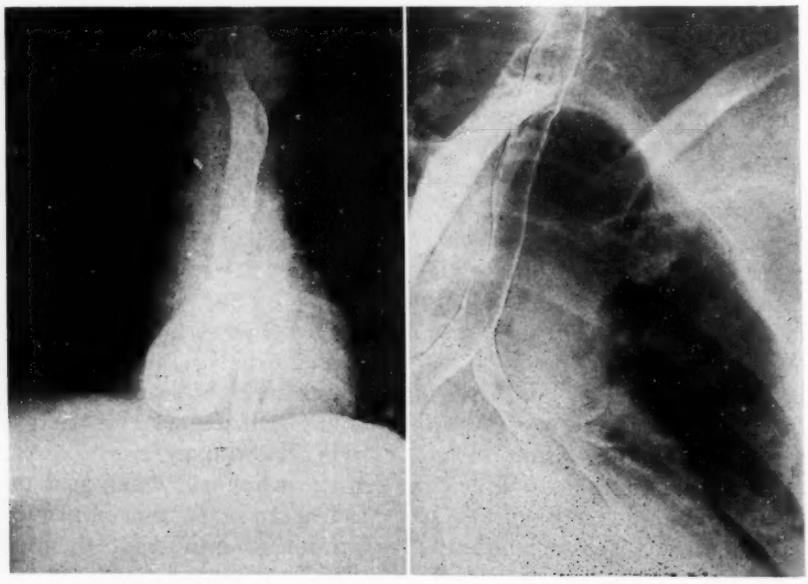
FIG. 7. A, grid-filtered half of chest x-ray showing improved contrast and definition due to reduction in secondary x-ray radiation. B, opposite half of chest showing the difference in the x-ray picture when taken without the use of a lead filter.

of aspiration pneumonitis (Fig. 8B), this procedure should never be neglected. However, special attention is advisable where aspiration pneumonitis appears due to difficulty in swallowing or where an esophagotracheal fistula is suspected. For investigating the latter possibility a spoonful of lipiodol is preferable to a barium suspension.

The information gained by observing a barium swallow is both direct and indirect. The former relates to the presence of intrinsic esophageal disease (e.g., tumor, spasm, stricture, diverticulum) while the latter is based on extrinsic influences affecting its function or its position (e.g., tumor pressure, constriction by a vascular ring, displacement by cardiac enlargement).

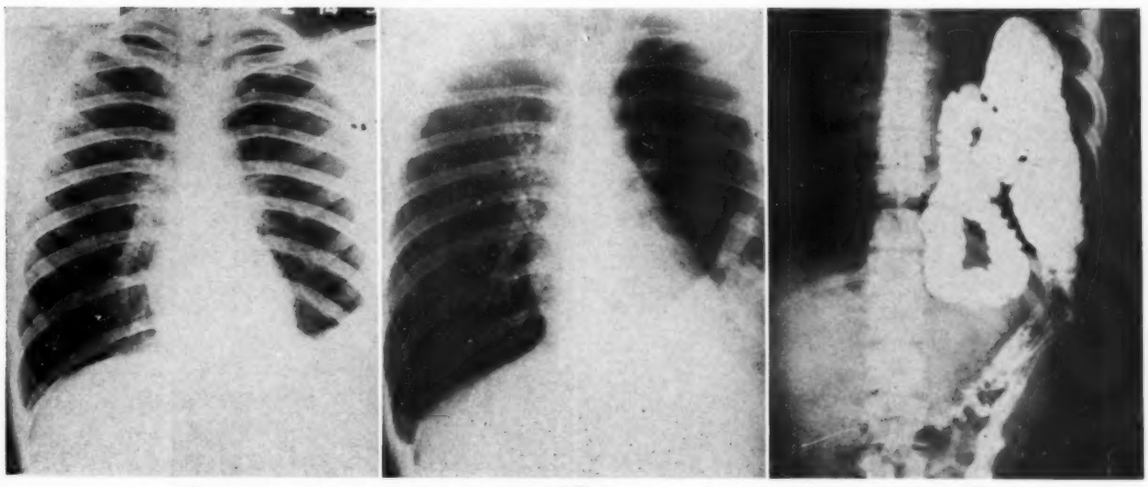
A *gastrointestinal x-ray series* and *barium enema x-rays* may also be required to differentiate a diaphragmatic hernia (Fig. 9) from other shadows in the lower lungs. In addition to a paraesophageal hiatus hernia the stomach may be involved in rupture through a congenital defect in the diaphragm. However, all barium studies may fail to demonstrate a diaphragmatic hernia when it includes only omental tissue.

A technic which requires some caution and experience rather than special equipment is *diagnostic pneumotborax*. Although the surgeon's skill has minimized the hazards of thoracotomy and all but eliminated the need



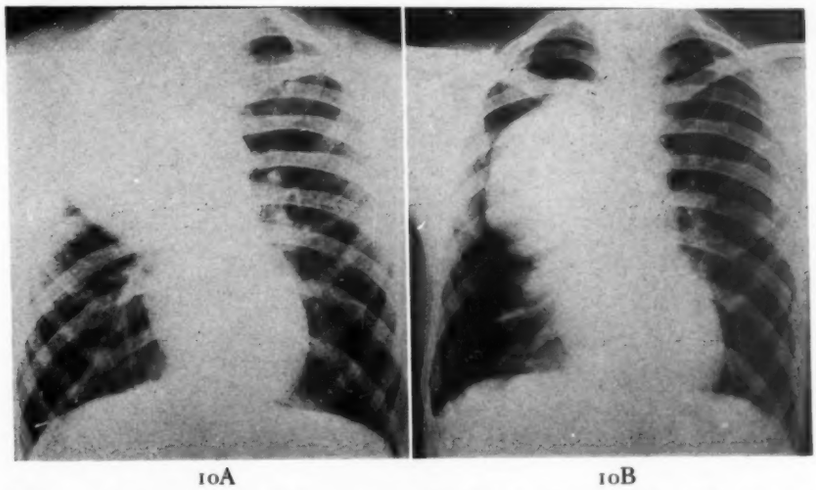
8A 8B

FIG. 8. A, esophagram showing a large diverticulum arising from the lower esophagus, thus explaining the patient's retrosternal distress. B, esophagram showing an overflow of barium with aspiration into the tracheobronchial tree due to swallowing difficulty which accompanied a neurologic disorder.



9A 9B 9C

FIG. 9. A, conventional chest x-ray (upright) with a shadow at the base of the left lung suggesting pleural fluid. B, conventional chest x-ray taken in left lateral recumbent position showing extension of fluid up along the lateral chest wall accompanied by areas of translucency suggesting large bowl. C, barium enema x-ray proving the existence of a defect in the posterior portion of the left diaphragm (not disclosed by diagnostic pneumoperitoneum or gastrointestinal x-ray series).



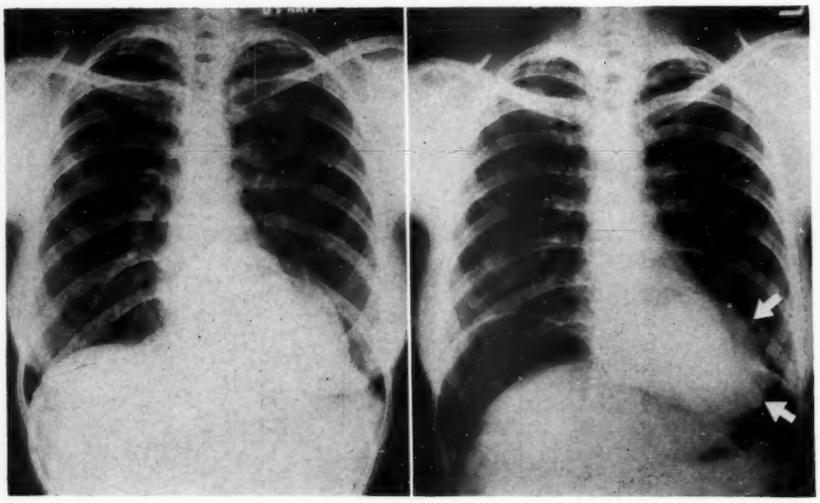
10A 10B

FIG. 10. A, conventional chest x-ray showing large tumor in right upper chest. B, diagnostic pneumothorax. Collapse of supporting lung results in sagging of tumor. Change in shape resembling a sac of fluid suggested the diagnosis of a large bronchogenic cyst (proved by resection).

for diagnostic pneumothorax, it may be well to review some of its aspects for those occasions on which it might still prove useful. If a small pneumothorax is to be induced, the needle should be inserted some distance from the lesion under investigation so as not to traumatize it or contaminate the pleural space. Aside from demonstrating the cystic nature of a tumor by its resulting change in shape (Fig. 10), pneumothorax helps to distinguish pulmonary from extrapulmonary lesions providing the surrounding pleura is not adherent.

A similar procedure which involves the introduction of air for tissue contrast is *diagnostic pneumoperitoneum*. Following this, x-rays taken in the upright position outline the undersurface of the diaphragm and help to distinguish a tumor (Fig. 11) from a local area of eventration. Demonstration of a hernia through the diaphragm by this method depends on the amount of air used and its postural localization in relation to the site of hernia. Diagnostic pneumoperitoneum can also fail to demonstrate a hernia which is completely surrounded by incarcerating adhesions.

Diagnostic pneumomediastinum is another



11A 11B

FIG. 11. A, conventional chest x-ray showing a large tumor in the left lower chest. B, diagnostic pneumoperitoneum. The tumor is dissociated from the abdominal organs by the subdiaphragmatic air, thus excluding hernia and proving the shadow to be located above the diaphragm (proved on removal to be a cystic neurilemmoma).

12A 12B

FIG. 12. A, pneumomediastinal planigram taken at a level through the superior vena cava (lower arrow). This vessel is outlined by air in the mediastinum. The jugular vein (left upper arrow) and the carotid artery (right upper arrow) are also outlined by air which ascended through the mediastinum. B, pneumomediastinal planigram taken at a level 1 cm. behind that shown in (A). The azygos vein (arrow) is surrounded and dissected away from the lateral tracheobronchial wall, by the mediastinal air.

technic which depends on the introduction of air contrast for the separation of tissues and the identification of their shadows. Introduced presacrally according to the method of Ruiz Rivas,[1,2] air ascends through the intercommunicating alveolar tissue spaces of the body to outline the surfaces of the diaphragm and some of the cardiovascular structures of the mediastinum. To obtain any appreciable information from such air in the mediastinum this procedure must be combined with sectional radiography. (Fig. 12.)

Sectional radiography is a method of study which has received increasing attention during the past decade. Referred to by many terms, such as planigraphy, tomography, laminagraphy, stratigraphy and body section roentgenography, it has also been characterized as a method of bloodless dissection. This procedure can be performed without difficulty in most offices which have standard x-ray equipment. By means of an attachment to the x-ray table, the film and tube move reciprocally in opposite directions during the exposure of each picture. Thus the shadows from a selected plane in the body fall on constant points of moving film, whereas shadows from above and below this level are projected onto constantly changing points of the film. The latter are consequently blurred or "erased" from view. With this technic lesions ordinarily obscured by overlying bone, soft tissue or other shadows become easily visible and their characteristics become more readily apparent.

Planigraphy reveals more clearly than other x-ray methods the presence of calcification within a tumor, thus helping to differentiate "tuberculomas" of lung and mediastinum from other tumors. It also helps to dissociate the complex lung root shadows and to distinguish between lymph node, tumor and normal pulmonary vessels. (Fig. 13.) This technic is very useful, too, in demonstrating the cause of obstructive pneumonitis when beyond the view of the bronchoscopist. In such instances it often helps to distinguish between an eroding calcified tuberculous lymph node and a small bronchogenic carcinoma.

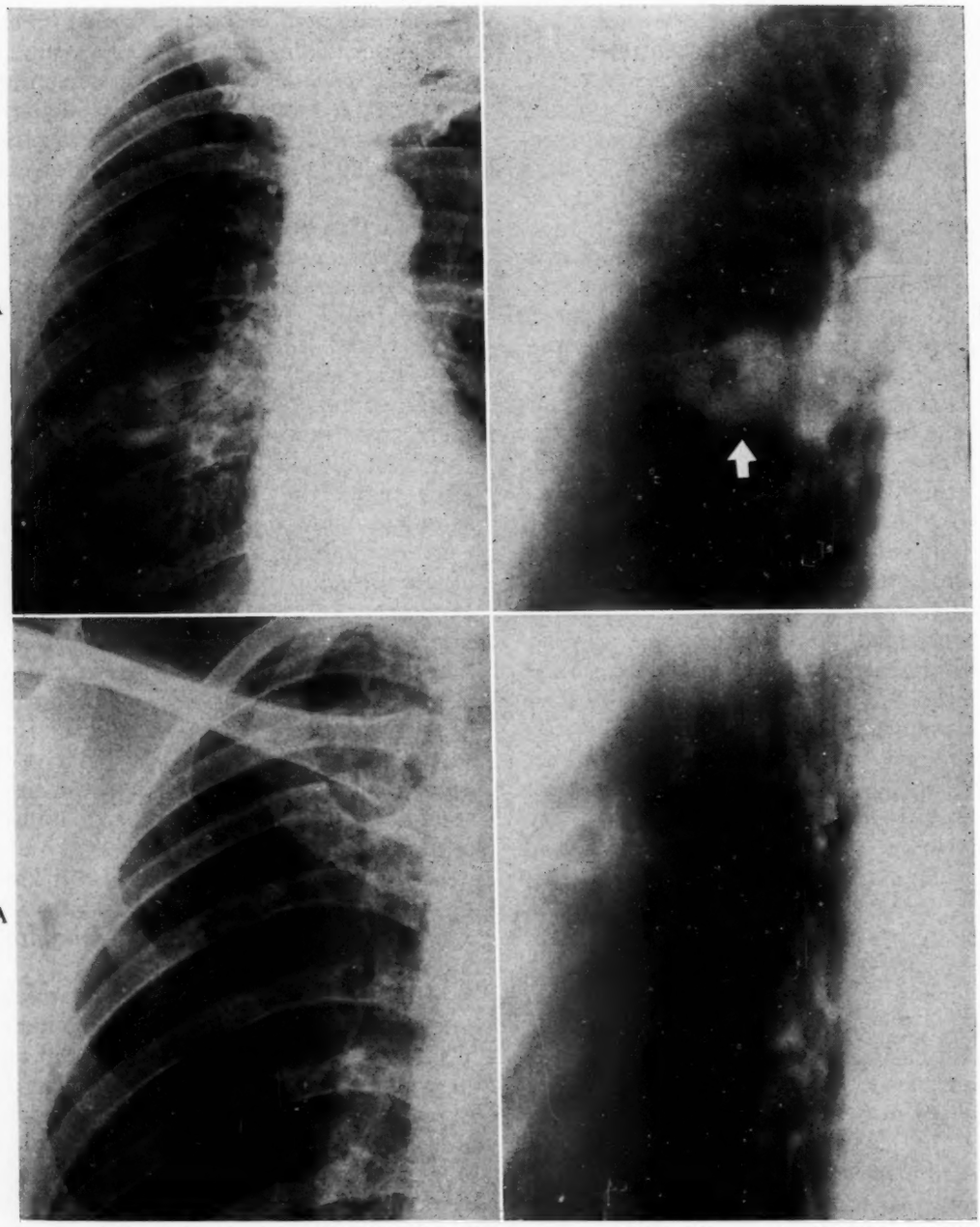
In tuberculosis, sectional radiography may not only help to detect an unsuspected cavity (Fig. 14) but also may demonstrate a much wider distribution of disease than suggested by the conventional chest x-rays. Applied to the lateral position this procedure offers the most accurate means for determining the segmental localization of tuberculosis as well as other parenchymal diseases. Sectional radiography is equally important in evaluating the results of medical therapy for tuberculosis since it can reveal a persistence of disease when there is no longer any evidence of such on the ordinary chest x-ray.

Among other important indications for planigraphy is the investigation of bone disease in the upper thoracic spine, ribs and sternum. This x-ray technic is also helpful in showing the true extent of bullous transformation of lung tissue and in distinguishing peripheral bleb formations from suspected pneumothorax. However, sectional radiography should not be relied on for demonstrating bronchiectasis or a residual lung abscess cavity, and for examination of the trachea and main bronchi it is secondary to bronchoscopy.

The only accurate method for determining the presence or extent of bronchiectasis is *bronchography*. While new media are constantly being tested, the iodized oils such as lipiodol and iodochloral® continue to serve as standard materials for this procedure. Umbradil and more recently dionisil have been available as water-soluble iodized substances offering as advantages the rapid absorption of their shadows. Aside from somewhat less satisfactory contrast and the need for rapid coordination of its bronchial instillation with the x-ray exposure, a substance like umbradil gives a false impression of the residua which remain in the lungs. The same precautions should be observed with reference to overfilling of the bronchial tree as with iodized oils; for while sufficient data may not yet be available in human beings, it appears that the base substance used in preparations like umbradil is retained for a considerable period after its iodine content has been absorbed. The same temporary influence on pulmonary function may therefore be expected as occurs following the use of iodized oils.

In most instances the degree to which characteristic residua persist following iodized oil bronchography should offer no difficulty in observing the course of the underlying disease. Excessive retention of such oil can usually be prevented by adequate cough control during bronchography, by avoiding cough depressants, by avoiding delays in one position during intrabronchial instillation, by avoiding use of too much oil, by prompt postural drainage and by administration of an ephedrine compound to prevent the trapping effects of bronchospasm following the procedure.

For dissociation and identification of the bronchi, as well as accurate localization of their diseases, the lateral chest x-ray is the most important one in bronchography. The oblique views which rank next in importance are usually not essential if good lateral pictures are available. The frontal (p-a) chest x-ray is a necessary complement to the lateral view,



13A 13B

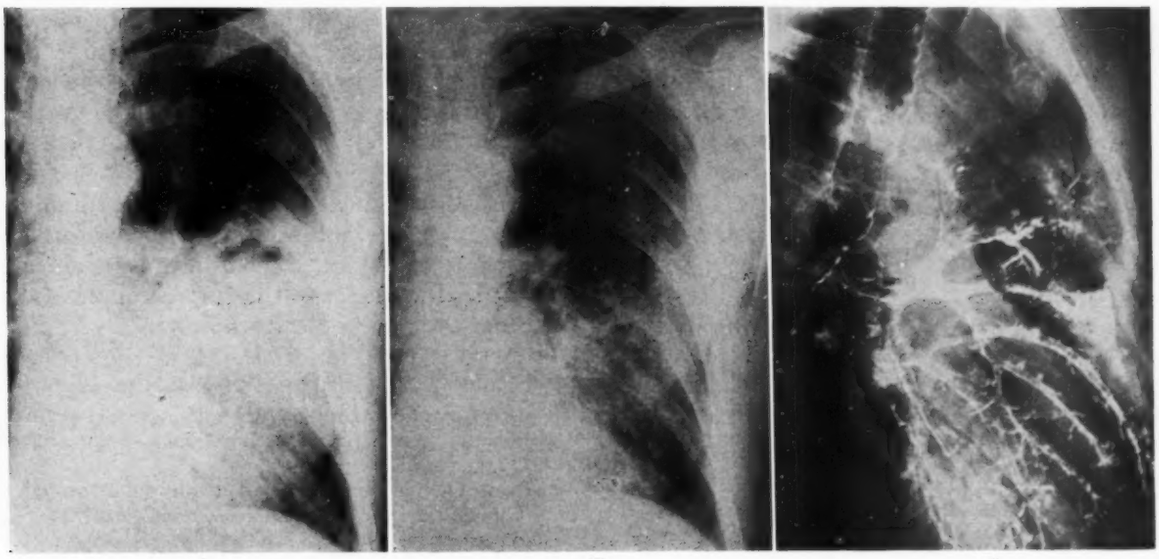
14A 14B

FIG. 13. A, conventional chest x-ray of the right lung showing an area of density associated with a ring-like shadow overlying the fourth anterior intercostal space and suggesting tuberculous or cystic lung disease. B, sectional roentgenogram (planigram) through the right lung of same individual reveals tumor mass (arrow) associated with enlargement of the adjacent bronchopulmonary lymph nodes. This suggested bronchogenic carcinoma (proved by resection).

FIG. 14. A, conventional chest x-ray of the right upper lung showing irregular infiltrations overlying the outer portion of the second anterior intercostal space. B, sectional roentgenogram (planigram) through a corresponding area of right upper lung reveals an unsuspected tuberculous cavity.

for together they reveal the three-dimensional changes in the bronchial tree and permit better correlation of the bronchogram with the conventional chest x-ray.

In addition to the generally accepted indications for bronchography in diagnosis and localization of suspected bronchiectasis there are a few other conditions in which this procedure is very helpful. The first of these is hemoptysis due to clinically unsuspected or so-called "dry" bronchiectasis. In such instances although bronchoscopy is negative,



15A 15B 15C

FIG. 15. A, conventional chest x-ray showing a large abscess in lingula division (superior segment) of left upper lobe. B, conventional chest x-ray following medical therapy suggested disappearance of the abscess but showed residual pleuroparenchymal changes. C, bronchogram (right anterior oblique position) revealed a large residual abscess cavity in the subpleural region of the left upper lobe (superior segment of lingula).

bronchography can establish the diagnosis. Another indication is the differentiation of tumor shadows due to ball-like fibrosis (to be published) from those due to malignancy. Still another indication is in demonstrating the persistence of a residual cavity following therapy for lung abscess. (Fig. 15.) In these cases bronchography is the only reliable method for revealing the source of a persistent cough, repeated hemoptysis or recurrent infections.

Perhaps one of the most dramatic technics in diagnostic roentgenology is *angiocardiography*. This procedure has proved to be a very valuable method for the study of cardiovascular abnormalities and their differentiation from other mediastinal conditions. Although some of its purposes in the diagnosis of congenital heart lesions are now better served by cardiac catheterization, it can be a helpful supplement to the study of such conditions.

Angiocardiography is a reliable means of demonstrating arteriovenous aneurysms in the lung and differentiating vascular shadows in the lung roots. The same may be said of those shadows which are due to aberrant pulmonary veins. However, in many of these latter conditions planigraphy can prove equally useful and more acceptable to the patient. In spite of the low mortality of angiocardiography, the unpleasantness of the experience coupled with its exacting requirements in equipment, personnel and teamwork makes this a procedure to be used only where other methods cannot serve adequately. It is the only diagnostic x-ray procedure which is advisedly performed in a hospital.

Fluoroscopy will be discussed elsewhere in this series of papers. Nevertheless, some comment on its relation to the foregoing technics seems warranted. For historical, technical and economical reasons the fluoroscope was widely used by itself in the early decades following Roentgen's discovery. However, it should now be considered only as an adjuvant to diagnostic roentgenography. The value of fluoroscopy in chest diagnosis is primarily to determine the functional aspects of a disease process and its influences, especially with reference to the heart, mediastinum and diaphragm. Although, as indicated previously, a good deal of such information can be recorded by inspiration and expiration roentgenograms, fluoroscopy may save considerable time and expense.

Two important cautions should be noted with regard to this procedure. First, no matter how assiduously one applies the principles of good fluoroscopy such as adequate dark adaption, the use of a Lysholm grid and the choice of minimum object-to-film distances, this procedure should not be relied on as a means of detecting or excluding pulmonary disease. Second, the fluoroscope is an instru-

ment with ultimately lethal potentialities to the physician who uses it. It should therefore be handled accordingly, observing the utmost precautions against the cumulative effects of exposure to its radiation. It is noteworthy to observe that as time passes and knowledge increases the so-called "safe" or "tolerance dose" to repeated x-ray exposure comes closer and closer to zero.

In conclusion, it is of interest to note the imminent release of a new type of special high speed x-ray screen. Developed by Dupont, these screens amplify the x-ray image to an extent that will make possible the reduction of x-ray exposure to approximately half what is now used for any method of examination. In extensive series of examinations this will significantly reduce exposure to the patient and will allow smaller x-ray units to operate with a capacity or speed of exposure previously attainable only with machines twice as powerful.

SUMMARY

This review in itself constitutes a summary of an extensive subject, and is therefore intended to serve only as a means of briefly orienting the reader to the current applications of diagnostic chest roentgenology.

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Bronchography in Pulmonary Disease

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BRONCHOGRAPHY is a method of diagnosis in pulmonary disease that apparently is not employed frequently enough. Along with physical examination, x-rays, planograms and bronchoscopy it has its place as a diagnostic procedure in pulmonary conditions. Lesions in the lung may be detected by examination and x-rays; bronchoscopy will reveal the condition of the bronchi and help in localization of the pathologic disorder; but a bronchogram will give information concerning the smaller bronchi that are beyond the areas visualized through the bronchoscope. The procedure is not an easy one, but with sufficient training and proper instruments the examination can be readily accomplished.

There is some difference of opinion in whose province the performance of the bronchogram belongs—the roentgenologist, laryngologist, endoscopist, chest physician or the thoracic surgeon. As a matter of fact it matters little who does the bronchogram as long as he becomes proficient in the procedure and has the proper equipment. There are many methods of obtaining a bronchogram. If the doctor will accustom himself to one of these according to his particular setup, and if he is able to obtain adequate results, it is of no consequence who does the procedure.

It is important for the student of bronchography to acquaint himself with the anatomy of the bronchial tree and to recognize the various bronchi and segments in the bronchogram. It would be well to study the charts that have been made available by Jackson and Huber and a number of textbooks.

INDICATIONS FOR BRONCHOGRAPHY

Bronchography is especially indicated whenever bronchiectasis is suspected. Actually bronchography is the only way one can make a certain diagnosis of bronchiectasis. The smaller bronchi are outlined so that their dilatation is demonstrated. The present treatment of bronchiectasis includes resection of the diseased portion of the lung. It is necessary, therefore, not only to establish the presence of dilatation of the bronchi in a certain area, but also to confirm the lack of pathologic conditions in normal portions of the lung. In other words the extent of disease must be demonstrated; bronchography can do this. It is best to bronchoscope these patients first in order to rule out any obstruction to the bronchi and to aspirate exudate that might interfere with proper filling of the branch bronchi.

In the bronchogram obstructive lesions show a blockage of the flow of the contrast medium. Partial obstruction to the bronchus is demonstrated by narrowing. Tumors, abscesses, cysts, bronchostenosis, pulmonary cavities and bronchial fistulas can be revealed, confirmed and localized by bronchography. It may be difficult to outline an abscess because the mucosa lining the bronchus may be edematous. However, an abscess may be recognized by abnormal distribution and rearrangement of the bronchi that surround it.

Tuberculosis is no longer considered a contraindication to the use of the procedure. Of course, it would not be wise to do a bronchogram in the presence of acute disease with fever, evidence of spread, etc.; but if the information obtained from a bronchogram is essential, the examination can be done without fear of complications. In these days of segmental resection for localized tuberculosis it is important to demonstrate the exact extent of disease and the areas that are normal. Following artificial pneumothorax it may be necessary to determine the condition of the bronchi in a lung or a part of a lung that will not expand. Then too, it may be important to know the condition of the bronchi when a lung appears to have cleared and the patient is about to be declared an arrested case.

CONTRAST MEDIA

We prefer to use lipiodol as the contrast medium. Recently water-soluble solutions have been used, but we have had relatively little experience with these preparations. They are rather quickly absorbed, and the material readily invades the alveoli which obscures the

picture unless the arrangement is such that x-rays can be taken immediately. Water-soluble contrast media are very irritating to the mucous membrane of the bronchi, producing cough which is not easily controlled even with an excessive use of the anesthetic. Water-soluble preparations are more viscid than lipiodol and cannot be used in lungs with limited function. The roentgen contrast is less than with lipiodol. However, the water-soluble media are absorbed within four hours; and if a repeat bronchogram is necessary, it can be done soon instead of waiting a week or two when lipiodol is used. Lipiodol may remain in the lung for several weeks.

Recently an oily suspension of water-soluble medium has been used. This reduces somewhat the amount of irritation to the mucosa but also delays the absorbability of material. Norris and Stauffer report good results using dionosil aqueous® which is less irritating to the mucosa and is not as readily absorbed into the alveoli.

Lipiodol should be used at body temperature. If it is too warm, it is more readily absorbed, "floods" the alveoli and obscures the picture.

PREPARATION OF THE PATIENT

The bronchographic examination may be performed on outpatients as well as hospitalized patients. Occasionally we encounter a reaction to the local anesthetic. This is greatly reduced by proper premedication which is only possible if the patients are institutionalized. We prefer, therefore, to have our patients hospitalized although with proper care the examination may be performed on ambulatory cases.

The patient is asked to omit the meal directly before the procedure. He is also asked to undergo postural drainage just before the examination if he has a great deal of exudate in the lungs. If postural drainage does not clear his lungs sufficiently, it is best to bronchoscope the patient and thoroughly aspirate the material before doing the bronchogram. However, we have found on occasion that the patient is more irritable after a bronchoscopy and is unable to withhold coughing so that a satisfactory bronchogram cannot be obtained. In this case the examination may have to be repeated.

An ambulatory patient should be given a barbiturate about an hour before and codeine a half hour before the procedure. The hospitalized patient is given nembutal 1½ gr. 2 hours before, and another 1½ gr. 1 hour before and codeine ½ hour before the bronchogram is done. If the patient is likely to salivate a great deal or has a great deal of exudate, atropine is added to the codeine. The premedication reduces the possibility of reaction to the local anesthetic and decreases the cough.

ANESTHESIA

There are a number of local anesthetics used in this work—cocaine 4 per cent, cocaine 10 per cent, pontocaine® 1 per cent or 2 per cent, butyn® 2 per cent, xylocaine, etc. For a long while we have had satisfactory results using a combination of 10 per cent cocaine and 2 per cent pontocaine which gives a solution of 5 per cent cocaine and 1 per cent pontocaine. The anesthesia must be given slowly in small amounts and with sufficient intervals between applications to obtain adequate results. The larynx and pharynx are sprayed with the anesthetic and then instilled with a laryngeal syringe into the trachea. The patient is asked to lean on one side and then the other to insure the dropping into each main bronchus. Small amounts are used but enough instilled to anesthetize the patient sufficiently to prevent coughing. We find the use of laryngeal applicators to the pyriform sinuses unnecessary and the use of anesthesia by aerosol unsatisfactory. The latter requires further instillations of anesthesia and is a waste of time.

VARIOUS METHODS OF BRONCHOGRAPHY

There are a number of ways of obtaining a satisfactory bronchogram. Each depends on the facilities available at the hospital or office in which it is done. The operator should choose a method suitable to his setup and training, and stay with it for the more one is accustomed to doing one method the better results will be obtained.

Supraglottic or Passive Method. This is the simplest method and is probably used a great deal in ambulatory patients who come to the doctor's office. The patient is in a sitting position. He is anesthetized. The tongue is held out with a piece of gauze and lipiodol is dripped from a laryngeal syringe placed at the base of the tongue. The patient is asked not to swallow and not to cough. He is asked to keep breathing or "pant like a dog." The lipiodol gradually runs around the epiglottis into the larynx and trachea. Another method of instilling the

lipiodol is to drip it from a laryngeal cannula directly into the trachea under indirect vision with a laryngeal mirror. Both lungs are filled by tilting the patient first to one side, leaning forward, then backward and then tilting to the other side and repeating the movements. About 10 to 15 cc. of lipiodol is used and films taken in the erect position. This is rather a "blind" method but is frequently satisfactory if one is interested in only the lower lobes and is not especially concerned about the upper lobes.

If one wishes to outline the upper lobes, the procedure is best done under fluoroscopic guidance so as to make sure to fill these areas adequately. One lung at a time should be done because of superimposition when taking lateral films. However, the patient does not usually care to return for another session and one is inclined to do both sides at the same sitting. Oblique films usually help in avoiding the effect of superimposed areas.

In outlining the upper lobes the lipiodol is instilled and the patient is placed in a recumbent position, with the head lower than the trunk, and turned to one side with the body almost prone. In this way the lipiodol will enter the upper lobe. The other side is outlined in a similar manner. The right middle lobe is filled while the patient is in an erect position and leaning forward and to the right. The filling is watched through the fluoroscope; and when proper outlining has been accomplished, films are taken in the reclining or erect positions according to the facilities. Anteroposterior, lateral and oblique views are taken in order to demonstrate all branches. About 20 cc. of lipiodol is used.

Deep breathing helps to spread the lipiodol to the small branches and it is important that the patient refrain from coughing. Lipiodol should not be used in great quantities and should not be instilled with pressure because it will tend to "flood" the alveoli. It is not necessary to fill the entire bronchial column. Covering the walls of the bronchi with a faint outline of lipiodol is sufficient for any study and is more satisfactory. Fluoroscopy should not be prolonged because the films must be taken as soon as possible after the instillation before "flooding" takes place.

Another method of filling the upper lobes is to have the patient seated and after tilting to one side to fill the lower lobe, he is brought forward so that the body and head are placed between his knees. This fills the upper lobe. The posterior portion of the lung is filled by leaning backward almost in a supine position. This is repeated on the other side. The method is useful when a tilt table is not available.

The patient is asked to cough under postural drainage technic after the x-rays are taken.

The supraglottic method is a simple one but not always satisfactory since it may be difficult to outline all the branches. Even under fluoroscopic guidance the lipiodol cannot always be properly directed.

Transglottic Method. This is perhaps the best method. A catheter is used for the instillation of the lipiodol and the course of the latter can be directed more adequately. It is a better way of filling the upper lobes.

The patient is anesthetized and in addition one side of his nose is sprayed. A No. 16 rubber catheter is passed through the nose to the pharynx. The tongue is held with a piece of gauze, and under deep breathing the catheter is slipped through the larynx into the trachea. The catheter may be directed into the larynx with the help of a laryngeal mirror and a long, curved forceps. If a preliminary bronchoscopy is performed, the catheter may be inserted through the nose and directed with the help of a direct laryngoscope. A coudé catheter with its firm end that is directed to one side is especially good for the procedure since it is more easily placed in the selected branches. The catheter is fastened to the nose with adhesive so that it is not coughed out. Additional anesthesia may be administered through the catheter if necessary.

The patient is placed on a fluoroscopic table, if possible a tilt table. The lipiodol is instilled on one side and the head of the table lowered. The lipiodol is seen to pass into the upper portions of the lung. The patient is turned on his side to an almost prone position. Lipiodol is slowly instilled at intervals during the maneuvers. No coughing or deep breathing is encouraged. If possible, spot films are taken in various positions. The other lung is filled in a similar manner and films taken. These may be supplemented by taking additional views with the patient in the erect position. Fluoroscopy should not be prolonged because of the tendency of the lipiodol to enter the alveoli and obscure the picture.

Subglottic Method. This is mentioned in order to be condemned. By this method the

trachea or cricothyroid membrane is punctured with a needle and lipiodol instilled. Subcutaneous emphysema may follow this procedure. It is an unnecessary risk.

Bronchoscopic Method. Lipiodol may be instilled through the bronchoscope at the time bronchoscopy is done. A small spiral-tipped tube may be used to place lipiodol into the branch bronchi. In this way one or two selected branches or areas may be filled when it is important to know the pathologic conditions in these without spreading lipiodol through the lungs. Spot films may be taken if the equipment is available.

BRONCHOGRAPHY IN CHILDREN

A considerable amount of patience, time, teamwork and good fortune is necessary in order to obtain adequate bronchograms in a child. The actual procedure is very similar to that performed in adults but is shunned by many of us because it is so extremely trying and time-consuming. However, the more one does, the easier it becomes to accomplish what one sets out to do.

Various methods of anesthesia may be used in children. Under four years of age it is possible to do a fast study under no anesthesia at all. Above the age of four years a bronchogram may be done under local anesthesia. Pontocaine, xylocaine or butyn which are less toxic than cocaine, may be used in lesser strengths and in smaller amounts and may be given by spraying or by nebulization. After spraying with the tongue out, the anesthesia is dropped on the base of the tongue and allowed to enter the larynx, trachea and bronchi. Either the supraglottic (passive) method or the transglottic (catheter) method may be used. The catheter should not be too large as it must not interfere with adequate airway in the glottis. Direct or indirect laryngoscopy may be necessary to insert the catheter. If required, additional anesthesia may be given through the catheter. Premedication in the form of a barbiturate and/or codeine and atropine should be administered in doses as required according to the age of the child. Fluoroscopic control may be used, the lipiodol distributed by assuming the aforementioned positions, and the desired films taken. If bronchoscopy or laryngoscopy is required, the lipiodol may be instilled through the scope and spot films taken. The procedure though extremely tedious in children is a great aid in diagnosing and often essential in treating various pulmonary conditions. Some like to do a bronchogram under general anesthesia, and in young children who are difficult to manage this may be the better way.

DANGERS IN BRONCHOGRAPHY

Sensitivity to local anesthesia is the most frequent difficulty encountered, but premedication and anesthesia in small amounts will help to alleviate this trouble. Iodism occasionally is encountered, but a history of this is usually obtained. The use of ACTH recently has been reported successful. Constant observation and as little lipiodol as possible should be used in patients with limited lung capacity. Infrequently lipoid pneumonia and the formation of granuloma are reported, but again this may be avoided by using as little lipiodol as possible. Do not insert lipiodol under pressure and avoid overfilling. Postural drainage is most important after the procedure. Of course, in the presence of an acute infection it would be unwise to perform a bronchography. In general relatively few dangers are involved in this procedure, and with extra precautions and extreme care the majority of them can be avoided.

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Angiocardiography in Pulmonary Disease

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IN 1938 a practical method of visualizing the chambers of the heart, the pulmonary circulation and the great blood vessels during life (now called angiocardiography) was introduced.[1,2] This was followed by detailed descriptions of the opacified cardiovascular structures in health and disease, so that in the ensuing sixteen years the importance of angiocardiography in clinical medicine has become established.[3–6] In this paper, recent and the more important uses of angiocardiography for the diagnosis and treatment of pulmonary disease, especially those amenable to surgical treatment, will be reviewed.

METHOD

Angiocardiography is a roentgen method of visualizing the cardiovascular structures. It is accomplished by making a rapid injection (1.5 seconds) of a concentrated organic iodide solution through the arm vein. Speed of injection is achieved by the use of a special needle-stopcock unit of 12 gauge, a special 50 cc. Luer-lock syringe with 12 gauge tip; and injection of the contrast substance with the arm elevated during inspiration.[2] Sodium uorkon® (sodium acetrizoate), 70 per cent, has been found to be the contrast medium of choice with the least side effects and reactions.[7] The dose of sodium urokon for children is 1 cc. per kg. of body weight; for adults, depending on weight, it is between 35 and 50 cc.

For angiocardiography of pulmonary disease in the adult, full size 14 by 17 inch films are necessary. In such cases, a standard stereocasette shifter may be used and will provide two films per injection. The circulation time in pulmonary disease is usually normal unless there is heart failure or cor pulmonale. Accordingly, exposures at 2.5 and 6.5 seconds after the beginning of the injection will in the majority of instances allow study of the pulmonary arterial and venous circulations. For children and adults of small stature the Fairchild 9 by 9 inch roll-film casette,[8] or the new 12 by 12 inch, F-X-R magazine,[9] will provide multiple (two per second) films during opacification of the cardiovascular system.

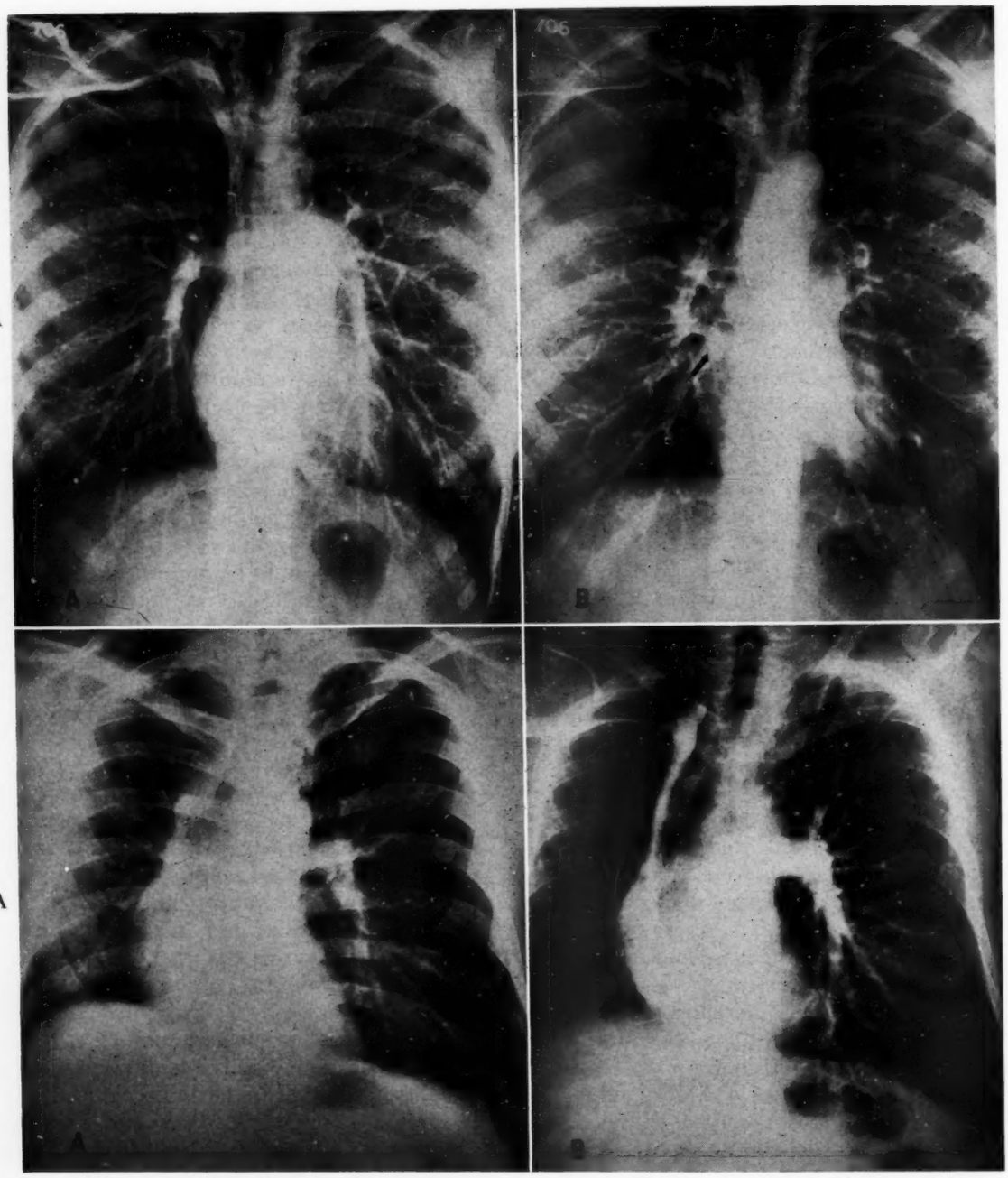
The erect postero-anterior (frontal) view is the best position for visualizing the pulmonary arterial and venous systems. (Fig. 1.) The lateral view is particularly desirable in localizing pulmonary vascular lesions in lobes or segments of the lung; oblique views aid the study of lesions affecting the right or left pulmonary artery. There should be no hesitation to give a second injection to secure lateral or oblique views; fatality has rarely occurred during angiocardiography for the study of pulmonary disease.

CONGENITAL ANOMALIES OF THE PULMONARY CIRCULATION

The role of the congenital pulmonary vascular anomalies in pulmonary disease is just beginning to be appreciated. Angiocardiography by delineating the pulmonary arterial and venous circulations makes possible the clinical recognition during life of many obscure anomalies. Diagnosis can then be followed by definitive treatment.

Absence of a Main Branch Pulmonary Artery. Either the right or left main branch of the pulmonary artery may be congenitally absent and the diagnosis of this newly recognized entity can often be made by conventional roentgenography.[10] There is displacement of the mediastinum (mediastinal herniation), trachea and heart by an overdistended lung while the opposite lung is hypoplastic and poorly vascularized. (Fig. 2A.) The angiocardiographic study (Fig. 2B) demonstrates absence of the right pulmonary artery and the circulation of the overdistended left lung. Other studies utilizing rapid serial roentgenography disclosed that the bronchial arterial circulation alone was responsible for the right lung vasculature.

Experience in three cases indicates that ab-



1A 1B

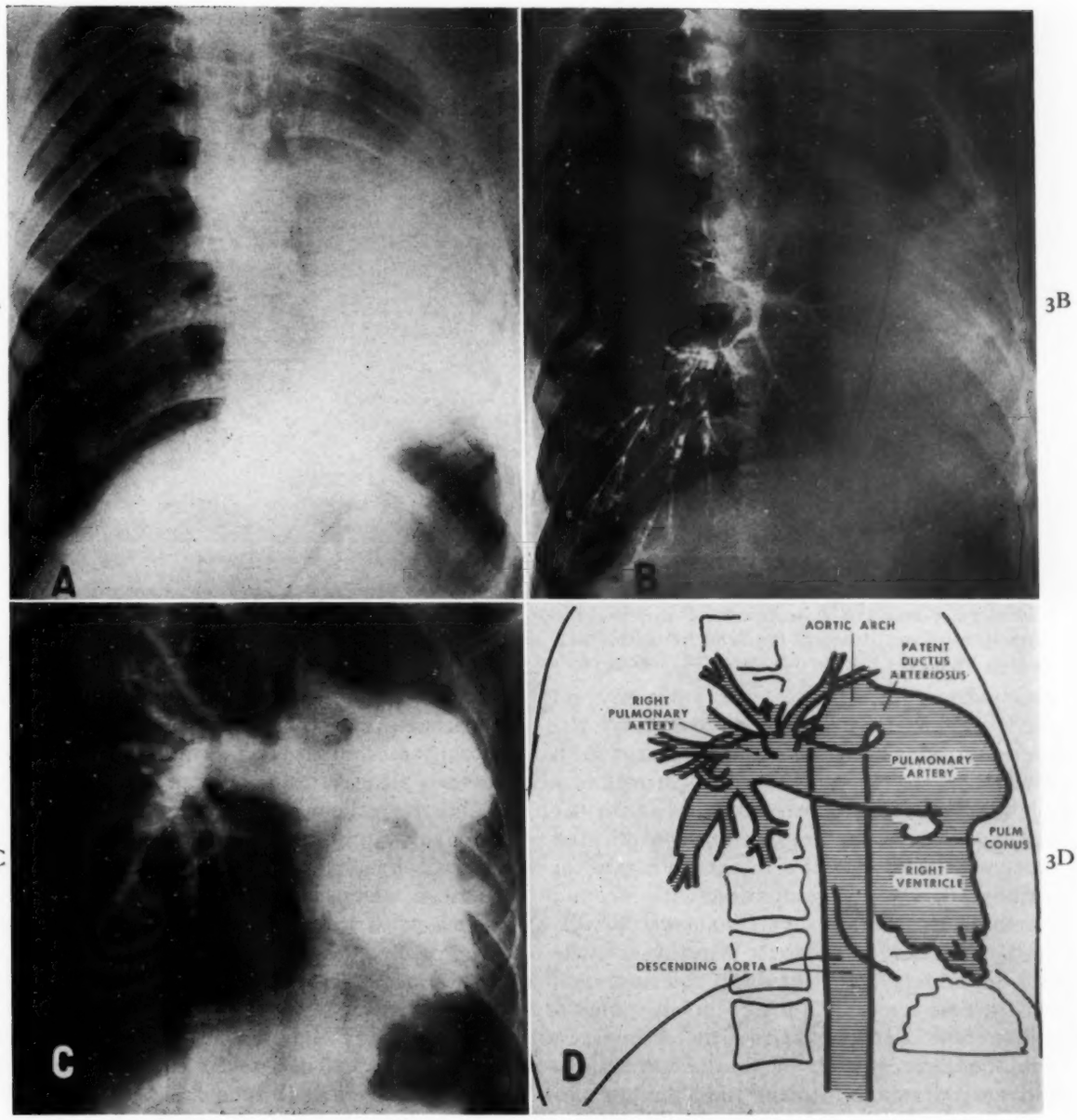
2A 2B

FIG. 1. The normal frontal angiocardiogram (twenty year old woman). A, opacification of right subclavian and innominate veins, superior vena cava, right atrium and ventricle, pulmonary artery (main stem, right and left branches) and pulmonary arterial tree is seen. B, the pulmonary venous system (arrow points to right inferior pulmonary vein), the left atrium and ventricle, and the aorta are visualized.

FIG. 2. Congenital absence right pulmonary artery (twenty-four year old man). A, conventional x-ray. There is displacement of the heart, trachea and mediastinum toward the right. Right lung is hypoplastic and vasculature is almost absent. B, angiocardiogram reveals an absent right pulmonary artery.

sence of a main branch pulmonary artery is usually discovered during routine chest x-ray survey. The condition may be mistaken for a mediastinal tumor. Limited experience indicates that this anomaly requires no treatment and that the prognosis is good. However, these patients must be kept under observation for the occurrence of pneumonia in the normal lung may raise havoc with the gaseous exchange processes.

3A



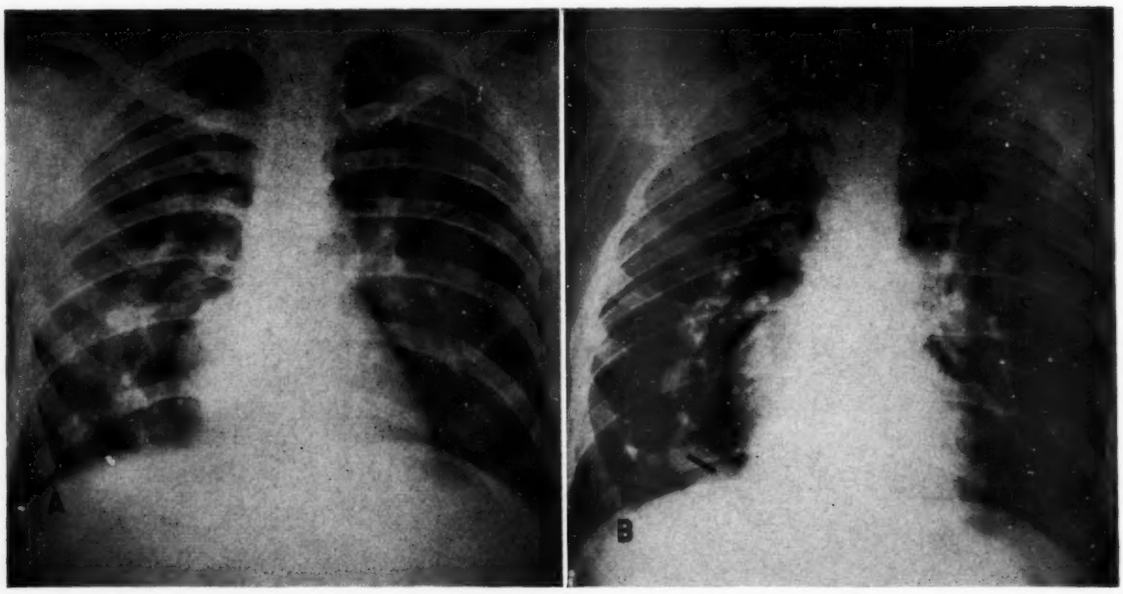
3B

3C

3D

FIG. 3. Agenesis left lung, patent ductus arteriosus with reversal of flow (twenty-two year old male). A, conventional x-ray shows opaque lower two-thirds left lung field with deviation of trachea, mediastinum and heart into left thorax. Aerated left upper third of lung is due to displacement of the right lung. B, bronchogram demonstrates absent left main bronchus. C, angiocardiogram reveals displacement and rotation of an enlarged right heart, a huge pulmonary artery and right branch (left is absent) and a patent ductus arteriosus. Simultaneous opacification of the descending aorta is demonstration of reversal of blood flow. D, tracing of C. From Lukas et al., *New England J. Med.*[11]

Absence of a main branch pulmonary artery also occurs in lung agenesis. The diagnosis of agenesis of a lung and differentiation from an acquired fibrothorax depends upon the demonstration by bronchography or bronchoscopy of a congenitally absent bronchus. The diagnosis should be suspected if there is an opaque shrunken thorax containing the mediastinal structures, heart and great blood vessels. (Figs. 3A, 3B.) In a twenty-two year old patient in addition to absence of the left pulmonary artery (Figs. 3C, 3D), there was also a markedly enlarged pulmonary artery and right branch due to pulmonary hypertension and a patent ductus arteriosus with reversal of the blood flow.[11] This complication makes ligation of the



4A 4B

FIG. 4. Anomalous right pulmonary vein entering inferior vena cava (twenty-two year old man). A, conventional x-ray reveals a crescentic shadow in lower part right lung. The right atrium is somewhat enlarged. B, angiocardiogram at time of left heart filling shows the crescentic shadow to be the right pulmonary vein (arrow) which enters the inferior vena cava. Courtesy of Paul B. Hoeber, Inc.[3]

ductus hazardous.[12] Recently, Maier and Gould[13] reported tracheal compression by the remaining pulmonary artery in an infant with agenesis of the lung. This mechanism may explain the cause of death early in life. In the adult, agenesis of the lung, unless complicated by a congenital cardiovascular anomaly or pulmonary disease, is compatible with life.

Anomalous Insertions of Pulmonary Veins. In 1949 partial anomalous insertion of the right pulmonary vein into the inferior vena cava was diagnosed during life by angiocardiography and cardiac catheterization.[14] Since then, recognition of totally anomalous pulmonary drainage into the right atrium and its tributaries has also become possible. Diagnosis of these conditions is important for the reanastomosis of pulmonary veins into the proper atrium in specially selected cases may be life-saving.[15]

Figure 4A is the classic conventional roentgenogram of a patient with a right pulmonary vein draining into the inferior vena cava. The crescentic broad vascular channels of the anomalous right pulmonary vein converging toward the cardiohepatic angle and inferior vena cava is clearly identified by the angiocardiogram. (Fig. 4B.) No treatment is indicated in such a case for the anomalous pulmonary venous circulation involves only one lung, and there are no cardiovascular complications. In such instances the patient is often asymptomatic and the condition is usually discovered after routine chest x-ray survey.

On the other hand, patients with partial anomalous pulmonary venous drainage complicated by a large interatrial septal defect, pulmonic stenosis or acquired rheumatic heart disease with mitral stenosis may be seriously handicapped and require surgery. Complete study, cardiac catheterization as well as angiocardiography is necessary for full evaluation.[15] Similarly, thorough study is indicated in patients suspected of having totally anomalous pulmonary venous drainage. When the anomalous pulmonary veins insert into the left innominate vein, a characteristic roentgen picture results. (Fig. 5A.) The abnormal mediastinal and hilar shadows have been likened to a "figure-of-eight,"[16] a "dumbell silhouette,"[17] a "mediastinal mustache"[18] and a "cottage loaf."[19] On angiocardiography (Fig. 5B) the widened mediastinal and hilar shadow on the left is seen to be due to the dilated common pulmonary venous trunk (persistent left superior vena cava) inserting into the left innominate vein; while on the right side, it is due to the dilated superior vena cava, enlarged because of the increased blood flow from the left innominate vein. The patient whose

roentgenograms are illustrated in Figure 5 was mistakenly diagnosed as having a lymphoma and given roentgen therapy at another hospital. This is the oldest (aged forty-two) recorded case in the literature. Polycythemia, residual left hemiplegia and congestive heart failure precluded corrective surgery.

Another patient with total insertion of pulmonary veins into the superior vena cava and right atrium had an associated atrial septal defect (in total anomalous pulmonary venous drainage this must exist for life).[15] The conventional chest roentgenogram suggested the diagnosis because of an anomalous appearing pulmonary vessel at the right base. (Fig. 6A.) Angiocardiography confirmed the diagnosis of anomalous drainage of the pulmonary veins. In addition, a newly recognized sign, a filling defect, at the site of insertion of the anomalous veins into the right atrium and ventricle was present. (Fig. 6B.) The filling defect is due to the turbulence created by the anomalous pulmonary venous blood flow. Surgical exploration, by Dr. Laurence Miscall, verified the presence of a common venous channel inserting into the right atrium and superior vena cava. Reinsertion of the pulmonary veins into the left atrium could not be done because of the underdeveloped left atrium and appendage (estimated as being one-tenth normal size).[15]

Anomalous Pulmonary Vessels from the Aorta. The surgical importance of anomalous systemic blood vessel insertions into the lung[20] and their relation to sequestration of the lung have recently been reviewed.[21] Through the courtesy of Dr. Herbert C. Maier a patient with anomalous abdominal aorta branches piercing the right diaphragm and inserting into the lung was studied. Figure 7 is a roentgenogram of a young patient who was disabled because of dyspnea. Angiocardiographic study (Figs. 7B, 7C) reveals the heart to be rotated into the right thorax while the right pulmonary arterial tree is hypoplastic. Figure 7D shows two branches of the abdominal aorta (arrow) piercing the right diaphragm and entering the lung. At operation, Dr. Maier ligated and divided the two aberrant arteries. Complete relief from the incapacitating dyspnea resulted and the patient was able to return to full physical activity. In this case, surgical treatment was done probably before infection and cystic degeneration of the lung (sequestration) occurred.

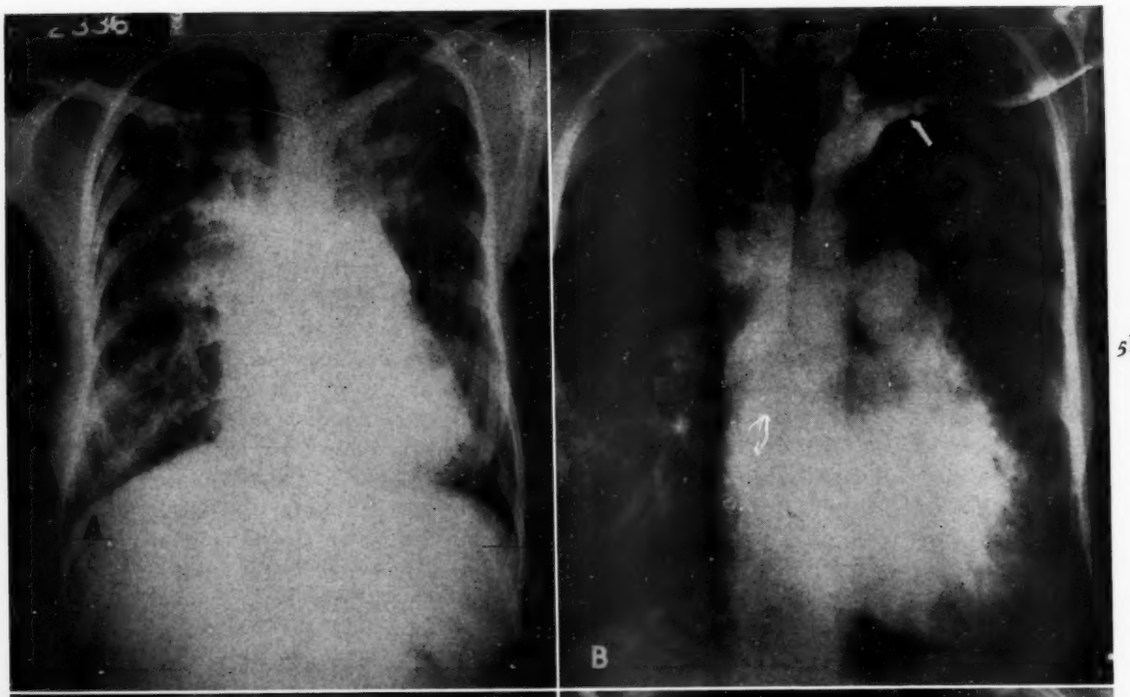
Pulmonary Arteriovenous Fistulas. A few years ago the existence of pulmonary arteriovenous fistulas was unknown. Since the advent of safe exploration of the lungs, angiocardiography, body section radiography and the fluoroscopic recognition of change in size of these lesions with respiratory maneuvers (Mueller and Valsalva), many cases have been recognized.[22] Pulmonary arteriovenous fistulas are of congenital origin and are closely related to hereditary hemorrhagic telangiectasis (Rendu-Osler-Weber's disease). Untreated cases of pulmonary arteriovenous fistulas run the risk of vascular thrombosis in that they may have unsaturated blood and polycythemia. Other complications are brain abscesses[23] and fatal hemoptysis.[24] For these reasons surgical excision of the pulmonary arteriovenous fistulas, especially if isolated and uncomplicated, even in the absence of signs and symptoms are advocated. At this center, a left upper lobectomy in one sibling and segmental resection of the apical segment of the right lower lobe in the other were done in two sisters who had pulmonary arteriovenous fistulas even though they were asymptomatic.[25] The curative and preventative features of this type of prophylactic surgery far outweigh the small operative risk.

Figure 8A shows the conventional roentgenogram of a patient who on routine chest x-ray showed the characteristic roentgen finding of pulmonary arteriovenous fistulas. A nodular parenchymal shadow at the right base connected with the pulmonary artery and an afferent vessel (a pulmonary vein) was present at its lower pole and proceeded toward the left atrium. Physical examination disclosed a vascular bruit. There was no polycythemia or cyanosis. Angiocardiography (Fig. 8B) clearly visualized the lesion and localized the arteriovenous fistula in the posterior basilar segment of the right lower lobe. At operation Dr. Frank Glenn found that ligation of the bronchial vessels was necessary to eliminate the bruit and thrill of the arteriovenous fistula and so lobectomy was done. The patient made an uneventful postoperative recovery. This, too, is an example of prophylactic thoracic surgery.

PULMONARY INFECTIONS

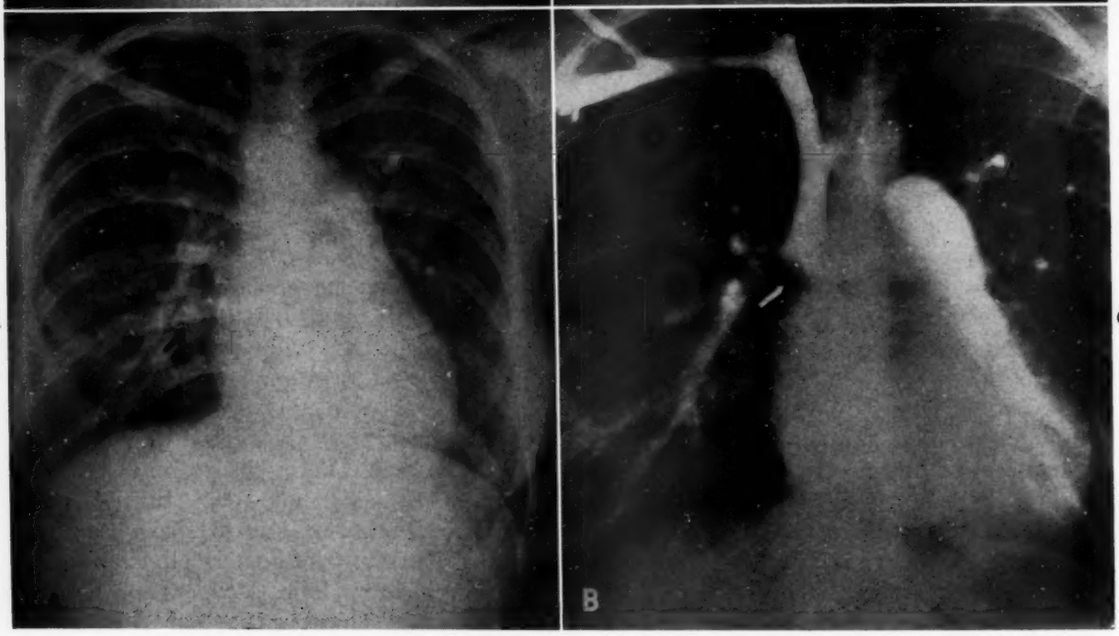
In pulmonary infection angiocardiography is mostly of academic interest. Verification of the presence of extensive pulmonary circulatory involvement, especially in the more chronic

5A



5B

6A



6B

FIG. 5. Total anomalous pulmonary veins inserting into left innominate vein (forty-two year old woman). A, conventional x-ray shows cardiac enlargement and enlarged supracardiac and hilar shadows. B, angiocardiogram at 1½ seconds via left arm, reveals deformity at site of insertion (arrow) of a dilated vessel (persistent left superior vena cava). The latter vessel and the dilated left innominate vein and the right superior vena cava are responsible for the enlarged supracardiac hilar and mediastinal shadows.

FIG. 6. Total anomalous pulmonary venous drainage inserting into the superior vena cava and right atrium (sixteen year old schoolgirl). A, conventional x-ray reveals an enlarged right heart and increased pulmonary vasculature. Arrow points to a prominent right inferior pulmonary vein. B, angiocardiogram at 2½ seconds, shows a filling defect of the superior vena cava and right atrium at site of anomalous pulmonary venous insertion. The right ventricle and pulmonary artery are enlarged.

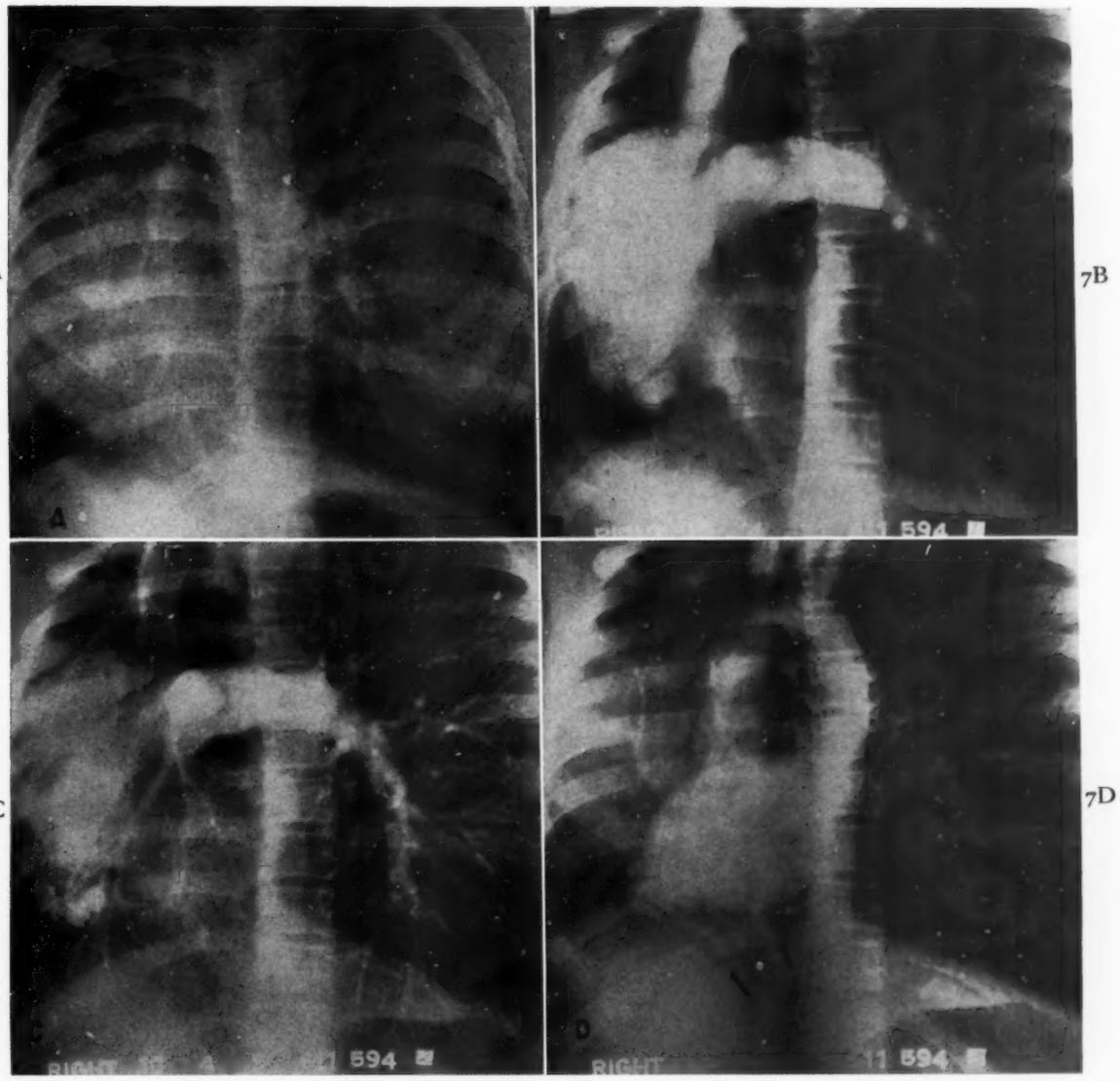


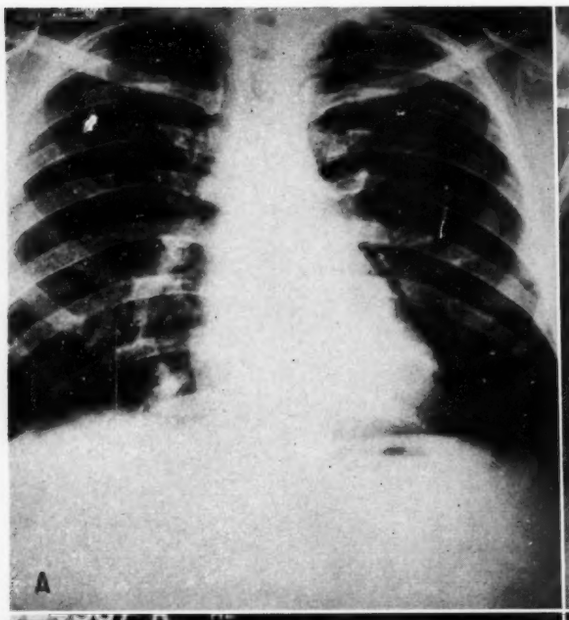
FIG. 7. Aberrant pulmonary vessels to right lung from abdominal aorta (fourteen year old schoolgirl). A, conventional x-ray shows hazy right lung with displacement of trachea, mediastinum and heart into right thorax. B, angiocardiogram at 1 second shows marked deviation of the superior vena cava, the right heart and pulmonary artery into the right thorax. C, angiocardiogram reveals the right pulmonary artery and branches to be hypoplastic. D, angiocardiogram demonstrates deviation and rotation of the left ventricle and aorta (assuming the left anterior oblique position). Arrows point to two anomalous abdominal aorta branches piercing right diaphragm into the lung.

lung diseases, can be obtained. However, abnormal diagnostic pulmonary vascular patterns have as yet not been recognized.

In pulmonary tuberculosis varying degrees of pulmonary avascularity depending upon the amount of lung tissue involved can be seen by angiocardiography. In the fibrothorax which sometimes follows the healing of pulmonary tuberculosis (Fig. 3), striking cardiovascular distortion may be shown. Similarly, in the collapse measures formerly commonly used in treatment of pulmonary tuberculosis (artificial pneumothorax, pneumoperitoneum, thoracoplasty and phreniclasia) a common feature has been diminution and deformity of the pulmonary vasculature.[26–29] Thoracoplasty, in particular, is probably especially effective by decreasing overdistention of the opposite lung. (Fig. 9.)

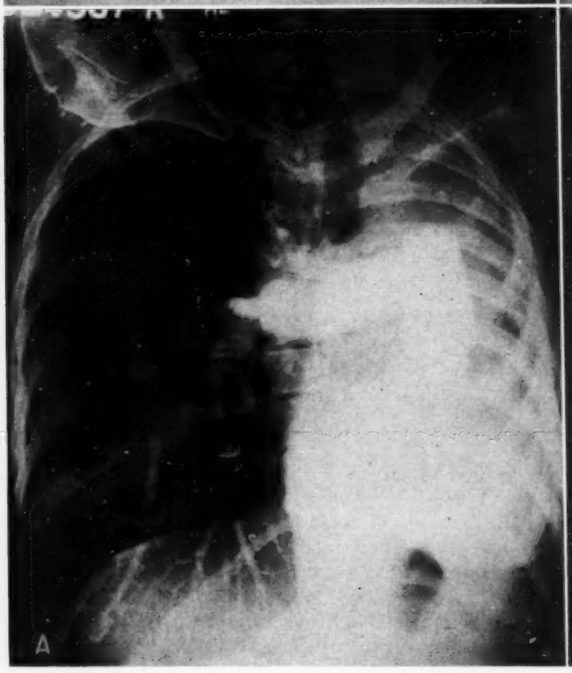
In bronchiectasis and lung abscess very little abnormality in the pulmonary vascularity can be demonstrated angiocardiographically until

8A



8B

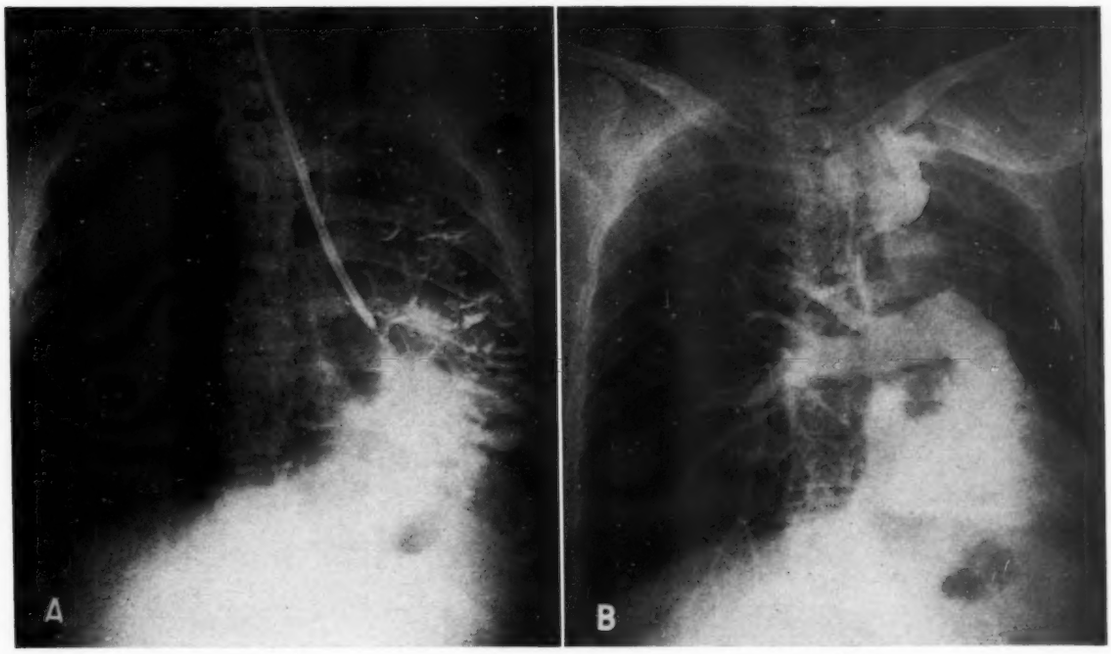
9A



9B

FIG. 8. Pulmonary arteriovenous fistula, posterior basal segment right lower lobe (fifty-four year old asymptomatic man). A, conventional x-ray shows the characteristic rounded density just above right diaphragm. Afferent pulmonary arterial and efferent pulmonary arteriovenous connections are present. B, angiocardiogram clearly identifies the aneurysm with its vascular connections.

FIG. 9. Left fibrothorax (tuberculous) treated by thoracoplasty (forty-two year old woman). A, angiocardiogram reveals marked tracheal, mediastinal and cardiac displacement (fibrothorax) which resulted after re-expansion of an ineffective pneumothorax for far advanced pulmonary tuberculosis. No left pulmonary artery was seen and there was marked overdistention of the right lung and pulmonary arterial tree. B, angiocardiogram following left thoracoplasty. The position of the pulmonary artery became more central and the right lung and pulmonary arterial circulation returned to a more normal position.



10A 10B

FIG. 10. Cystic bronchiectasis, left lung (forty-two year old man). A, bronchogram demonstrates cystic bronchiectasis, left lung and fibrothorax. B, angiocardiogram reveals marked rotations of the heart. The left pulmonary artery is not visualized. Courtesy of Paul B. Hoeber, Inc.[3]

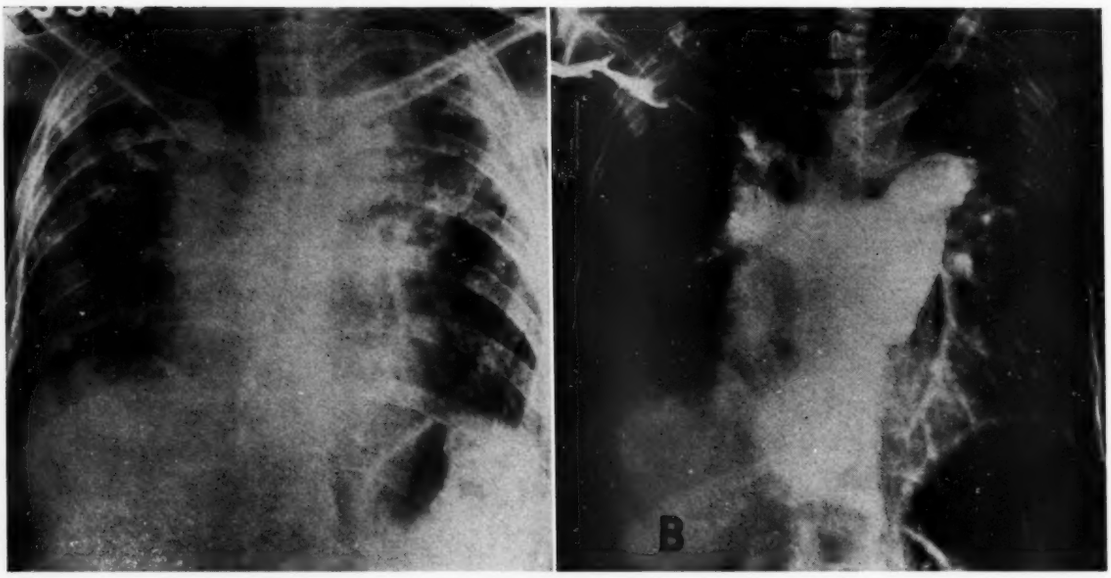
there is extensive pulmonary fibrosis.[3] Figure 10 shows absence of the left pulmonary arterial circulation in a patient with unilateral cystic bronchiectasis associated with fibrothorax of the left lung.

PULMONARY FIBROSIS

Pulmonary fibrosis is not uncommon in lung disease. It follows many pulmonary chronic infections like tuberculosis, bronchiectasis and lung abscess. It occurs in the pneumoconioses, varying from the fine granulations of anthracosis to the coarse nodulations of silicosis; in granulomatous lung disease (Boeck's sarcoid); and in the collagen diseases that affect the lung such as scleroderma.[30] In such cases, the effect of the fibrosis in obliterating the pulmonary vascular bed and causing pulmonary hypertension and cor pulmonale must be kept in mind. One of the earliest signs in the development of pulmonary hypertension is enlargement of the pulmonary artery and branches. Detection of enlargement of the pulmonary artery and branches may be difficult by conventional roentgenography but easily accomplished by angiocardiography. Angiocardiography, by demonstrating the large size of the pulmonary artery and main branches, may therefore give the first hint of the development of pulmonary heart disease.[3,31,32] Such was the case in an elderly woman with progressive pulmonary fibrosis (Fig. 11A) in whom enlargement of the hilum was thought to be due to either sarcoid involvement of the hilar lymph nodes or the development of a pulmonary neoplasm. Angiocardiography (Fig. 11B), however, disclosed an enlarged pulmonary artery and branches which reflected the pulmonary hypertension and the compensated cor pulmonale which had developed secondary to the pulmonary fibrosis. Visualization of an unfolded arteriosclerotic aorta also ruled out the presence of an aortic aneurysm.

DIFFERENTIATION OF PULMONARY, MEDIASTINAL AND HILAR MASSES FROM ANEURYSM

Enlargement or aneurysm of the great vessels (superior vena cava, pulmonary artery and aorta) may, because of their hilar and mediastinal locations, simulate pulmonary or mediastinal disease. An example of enlargement of the superior vena cava (right and persistent left) is present in Figure 5, wherein completely anomalous pulmonary veins drain into the left innominate vein. Enlargement of the pulmonary artery and branches secondary to pul-



11A 11B

FIG. 11. Pulmonary fibrosis associated with pulmonary heart disease (sixty-four year old woman). A, conventional x-ray shows widespread pulmonary fibrosis with mediastinal and hilar enlargement. B, angiocardiogram reveals the mediastinal and hilar widening to be due to enlargement of the pulmonary artery and branches (compensated cor pulmonale).

monary fibrosis is seen in Figure 11. Syphilitic aortic aneurysms are fortunately becoming rare. Because of their intimate hilar and mediastinal situation they may compress or occlude major bronchi causing pulmonary suppuration and fibrosis and simulate lung cancer. In such instances, angiocardiography by revealing the aneurysm will establish the diagnosis and make thoracotomy unnecessary,[3,33–35]

MISCELLANEOUS PULMONARY DISEASES

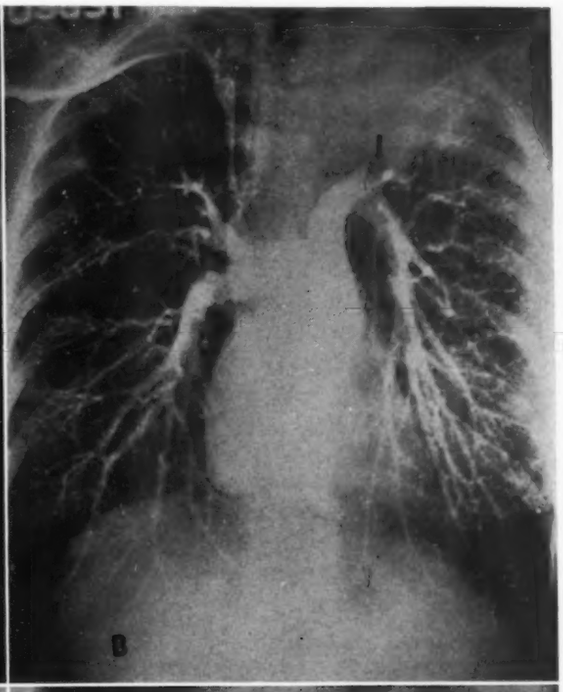
In varied pulmonary disease angiocardiography has demonstrated during life pulmonary vascular lesions which previously could only be suspected from conventional roentgenography. Here again, angiocardiography is mostly of academic value in that it provides a better understanding of the pathologic process. Absent pulmonary vasculature beginning abruptly in major or segmental pulmonary arteries has been demonstrated in patients having a pulmonary embolus.[3] In another patient with a chondroma occluding the right lower lobe bronchus, markedly diminished circulation was present. Following bronchoscopic removal of the tumor, the right lower lobe circulation returned to a normal state.[3] In contrast to the decreased circulation in chronic pneumonitis that is associated with bronchiectasis, chronic lung abscess and aspiration pneumonia, (which probably reflects the degree of fibrosis that accompanies the chronic pneumonia); the pulmonary circulation in acute pneumonia remains unaltered.

Marked deformity of the pulmonary artery, branches and tree, secondary to the pulmonary changes, may occur in thoracic deformity, especially kyphoscoliosis.[36] In generalized emphysema a "winter tree" pattern with wiry secondary and tertiary branches may be seen.[3] Characteristic crowding together of lobar or segmental pulmonary arterial vessels can also be seen in atelectasis. (Fig. 12.) In pleural mesothelioma deformity of the main pulmonary artery is a feature of the diffuse malignant type.[37] In diffuse metastatic neoplastic involvement of the lung no vascular abnormality is seen. Metastatic involvement of the mediastinal structures, however, may result in deformity of the great vessels (superior vena caval and pulmonary arterial) and be recognized after angiocardiography.[3]

BULLOUS EMPHYSEMA

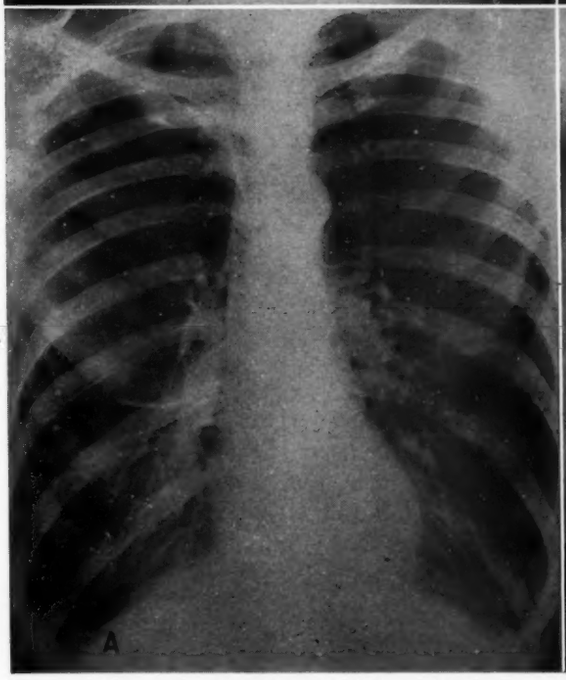
Bullous emphysema is believed to be due to localized subpleural vesicular emphysema which arises within the lung parenchyma from a conglomeration of distended vesicles. The bullae may vary in size from small air sacs to huge balloon-like structures involving a whole

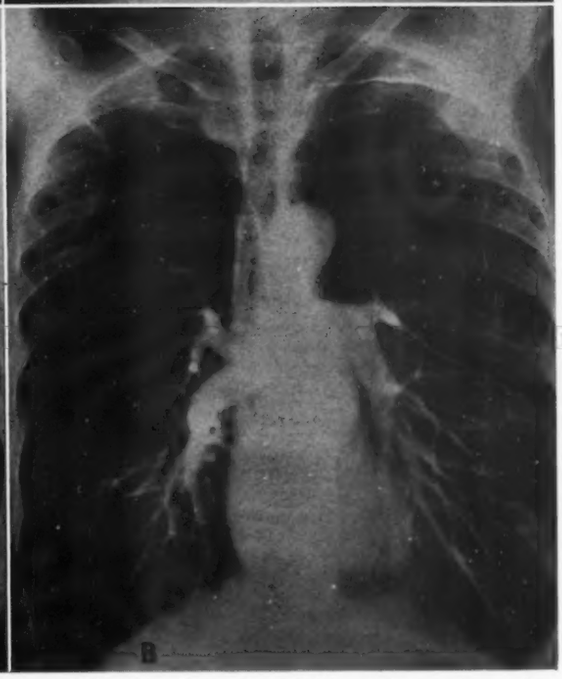
12A



12B

13A





13B

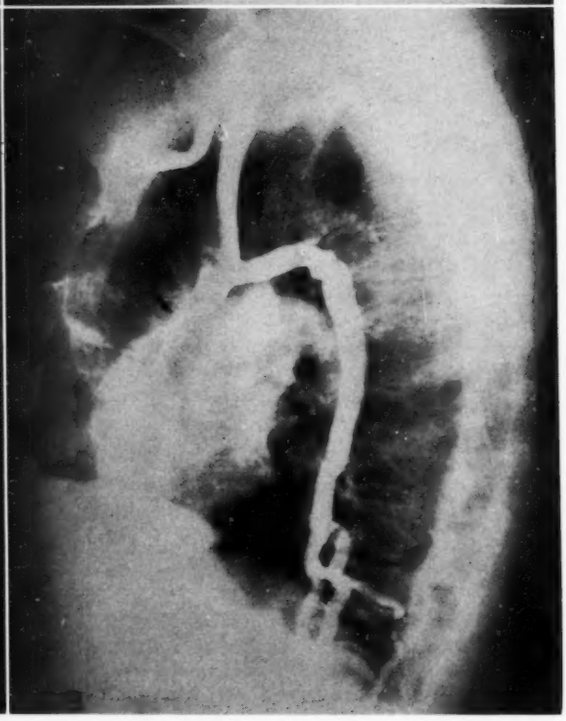
FIG. 12. Two cases of atelectasis right and left upper lobes of the lung due to bronchial carcinoma. A, angiocardiogram reveals crowded right upper lobe circulation (arrow) in an atelectatic right upper lobe due to bronchial cancer. B, atelectasis due to carcinoma occluding the left upper lobe bronchus. Arrow points to filling defect caused by destruction of the apical-posterior segmental branch of the left ascending pulmonary artery. In both instances surgical resectability can be predicted by the angiocardiogram.

FIG. 13. Bullous emphysema, upper lobes (fifty-three year old man). A, conventional x-ray shows voluminous lungs with huge bullae of upper lobes. B, angiocardiogram shows marked upper lobe avascularity with crowding of the lower lung circulation at bases. Left lobectomy and removal of bullae (by Dr. Laurence Miscall) afforded considerable relief of dyspnea and permitted patient to return to work.

14A

14B

15A

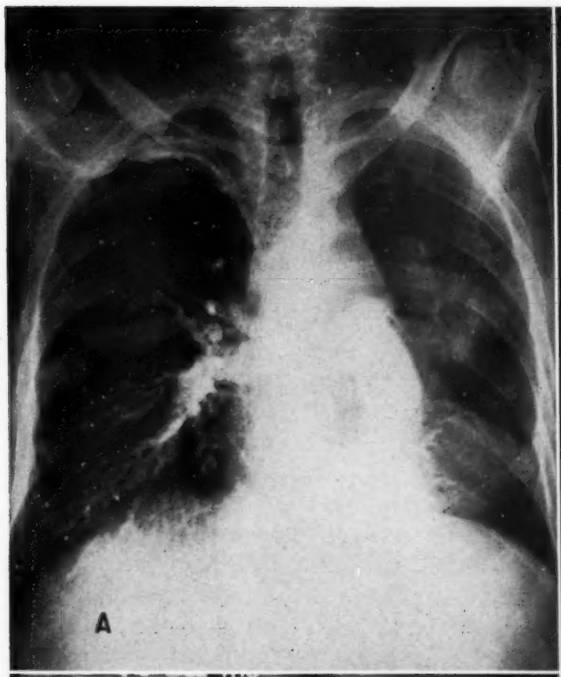


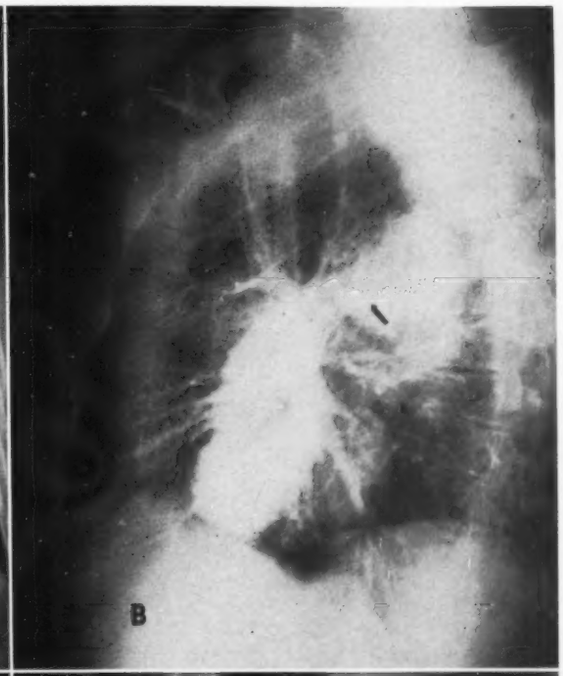
15B

FIG. 14. Superior vena caval syndrome due to cancerous obstruction and invasion of superior vena cava (forty-nine year old man). A, conventional x-ray shows widening of anterosuperior mediastinum. No pulmonary disease was demonstrated by x-ray and thoracotomy. B, angiocardiogram revealing intraluminal superior vena cava obstruction and deformity due to cancer, primary in right lung (proved at necropsy).

FIG. 15. Carcinoma right lung causing superior vena caval and right pulmonary artery occlusion (fifty-three year old male). A, angiocardiogram (arrow) reveals superior vena caval and right pulmonary artery occlusion due to cancer at right hilum with resulting azygos system collateral circulation. B, lateral angiocardiogram shows deformity of the superior vena cava (arrow), absent right pulmonary artery and the dilated vena azygos system.

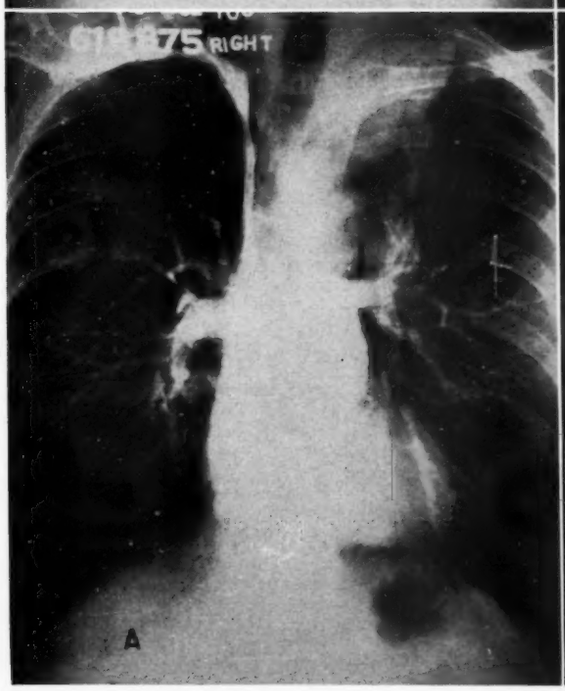
16A

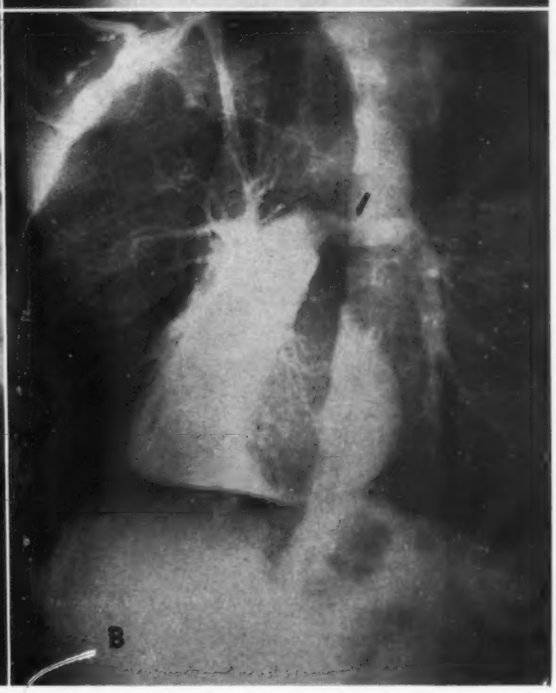




16B

17A





17B

FIG. 16. Complete left pulmonary artery occlusion by cancer of lung (fifty-seven year old man). A, frontal angiocardiogram reveals an absent left pulmonary artery (arrow) due to cancer involvement. B, left anterior oblique angiocardiogram demonstrates the absent left branch (arrow) at bifurcation of the main pulmonary artery.

FIG. 17. Partial occlusion left pulmonary artery by lung cancer (fifty-three year old man). A, angiocardiogram shows deformity (arrow) and reduction in size of left pulmonary artery. B, lateral angiocardiogram shows the dwarfed left pulmonary artery and site of narrowing (arrow) produced by the cancer.

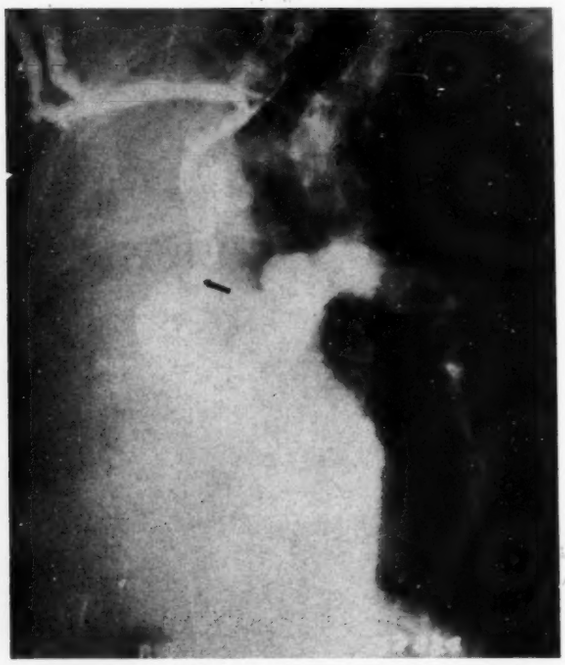


FIG. 18. Polypoid invasion superior vena cava following right pneumonectomy for cancer of lung (fifty-one year old male). Angiocardiogram reveals polypoid deformity of the superior vena cava (arrow) due to recurrence of cancer.

or most of both lungs. Symptoms may be lacking and the condition revealed by routine chest x-ray examination. Patients with extensive bullae, especially those with associated generalized emphysema, fibroid tuberculosis, bronchiectasis and pulmonary fibrosis of varied etiologies, may, on the other hand, be quite dyspneic and totally disabled. They are also liable to have spontaneous pneumothorax which in the presence of disease in the opposite lung may be catastrophic.

Studies now being made, suggest that bullous emphysema is often a progressive disease which is liable eventually to destroy enough lung structure to produce what has been termed "the vanishing lung." To cope with such an eventuality, surgical excision of bullae, before they have become massive and require lobectomy is being advocated.[38,39]

Angiocardiography has been found useful to assess the state of the pulmonary circulation in bullous emphysema. Often the conventional chest x-ray (Fig. 13A) fails to reveal the true extent of the bullae, for lung markings from neighboring lung tissue may be seen through the transparent air sacs. Opacifying the pulmonary circulation (Fig. 13B) will often clearly delimit the bullae as they are devoid of circulation. Furthermore, the crowding of the pulmonary circulation toward the bases, as shown in Figure 13B, demonstrates the degree of compression of functioning lung tissue. Angiocardiography in bullous emphysema may, therefore, be used as a guide to the selection of the cases suitable for surgery. Functional reexpansion of the lung and return of the lung and the pulmonary circulation to its proper location has followed surgical excision of bullae. Marked symptomatic improvement permitting the patient to return to work has resulted.[39]

LUNG CANCER

The importance of angiocardiography in lung cancer can be inferred from a recent angiocardiographic study of 100 cases. In 87 per cent there was involvement of the great blood vessels (superior vena caval and pulmonary arterial systems). In almost one-half of these (42 per cent) the invasion or occlusion of the pulmonary artery and the superior vena cava system was at major sites which made it doubtful that surgical attack might affect cure.[40]

Invasion of the superior vena cava by lung cancer is shown in Figure 14. Occlusion of the superior vena cava with resultant collateral circulation through the vena azygos system is seen in Figure 15. In addition the cancer has occluded the right pulmonary artery proximal to its bifurcation into the ascending and descending branches. Occlusion of the left pulmonary artery as it emerges from the main stem pulmonary artery is demonstrated in Figure 16. Marked deformity with obstruction of the left pulmonary artery at the hilum is depicted in Figure 17. In contrast to the foregoing serious major vessel involvement, lobar (Fig. 12A) and segmental (Fig. 12B) pulmonary arterial involvement are favorable signs for operation.[3,40,41]

Angiocardiography may also prove useful in assessing the results of radiation and surgical treatments. Figure 12A is the x-ray of a patient who had atelectasis of the right upper lobe due to carcinoma involving the bronchus. He refused operation and was treated by x-radiation. Angiocardiography following completion of the course of treatment showed complete reaeration of the right upper lobe and he has been free of evidence of recurrence for three years. On the other hand, a patient who

had a pneumonectomy because of right lung cancer (Fig. 18), soon began to show clinical evidence of superior vena cava obstruction (superior vena cava syndrome). Angiocardiography revealed recurrence of the cancer in the right thorax with superior vena cava invasion.

Superior vena cava and major pulmonary artery invasion, stenosis and occlusion are not pathognomonic of lung cancer. Similar lesions have been produced by lymphoma and syphilitic aneurysm.[3,42] Segmental and lobar pulmonary artery derangement also occurs in many pulmonary diseases (infection, fibrosis, emphysema). Accordingly, assessment of the role of the vascular lesions must only be made when cellular or biopsy proof of lung cancer is available. Only then will the information provided by angiocardiography aid the surgeon to plan the attack on the neoplasm.

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Reliability of Chest Radiography in the Diagnosis of Pulmonary Lesions

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THE purpose of this paper is to provide a review of recent studies on the reliability of interpretation of chest roentgenograms. Such interpretations are among the most valuable tools available to the clinician and surgeon in the diagnosis and treatment of pulmonary disease. Much of the progress in medical diagnosis and a great share of the advances in surgery are traceable to the discovery and development of roentgenology.

Radiography fulfills its functions best when it is used as a diagnostic aid, that is, as an instrument for providing valuable evidence of disease which must be integrated with other clinical and laboratory findings. In practice, however, it sometimes happens that the interpretation of a roentgenogram is accepted as definitive and decisive, and is relied upon as a sole guide in diagnosis and treatment. Such a course of action overlooks the limitations and errors inherent in any human activity.

Observer error is known to exist in the perception of objects which are much more tangible than an x-ray shadow. Considerable variation may therefore be expected in radiographic interpretations and in other clinical methods and procedures. Indeed, when put to the test, all are found to exhibit variability of much greater magnitude than had previously been suspected.[1–5] Our knowledge of subjective errors in clinical medicine and in the different diagnostic tests is, however, meager. Because the problem can be more easily studied in radiography, more precise data are available in this than in the other fields of medicine.

One of the benefits which result from the demonstration and quantitative evaluation of observer error in chest radiography is that it provides a stimulus for devising methods to reduce its magnitude. From a long-range point of view, these call for fundamental studies relating to film interpretation, the perception and classification of shadows, which ultimately will lead to greater consistency and reliability. More immediate results, however, have already been attained by utilizing present knowledge. Thus it was demonstrated that, at least in case-finding activities, the undesirable effects of false diagnosis can be reduced significantly by the employment of dual reading of all survey roentgenograms. This procedure has been adopted as the method of choice by many forward-looking agencies conducting such activities. Whether an extension of dual reading can be useful in clinical radiography and in its application to surgery has not yet been tested objectively, but it can be inferred indirectly from the other studies. It is, however, likely that the studies have had some beneficial effect on clinical radiography because of the stimulus they provide for increased use of consultation and multiple interpretation in the more difficult cases.

GENERAL CONSIDERATIONS

Evaluation studies of diagnostic procedures are of relatively recent origin, and neither methodology nor terminology have been stabilized. It is important, therefore, to define the various terms used, or at least to clarify their meaning sufficiently to avoid gross misunderstanding. Accordingly, the following statements are presented as explanatory notes on the meaning of some of the terms as they will be used in this discussion. These should not be considered as precise definitions.

Diagnosis. The process of identifying a disease by consideration of history, symptoms, physical signs and results of special tests. It is derived by a process of integration and utilization of all pertinent facts in a given case. Diagnosis in this sense was rarely if ever the subject of evaluation studies.

Diagnostic Test. A test, the findings of which are useful as aids in diagnosis, or as a means for distinguishing between individuals

who may possess a certain disease or condition and those who are free from the disease or condition. In general it is the diagnostic test which is being evaluated in most studies on "diagnosis."

Validity of a Diagnostic Test. The correlation between the findings of a diagnostic test and the presence or absence of the disease or condition in the individuals examined. The validity of a diagnostic test cannot be established by the use of the test alone; it must depend on additional examinations, tests and data provided by sources other than the diagnostic test under study.

Reliability of a Diagnostic Test. The ability of the test to reproduce its findings and to provide consistent results in repeated examinations. The reliability of a given test can be studied independently of the results of other tests and other sources of information. The determination of the reliability of a diagnostic test is a prerequisite to the evaluation of its validity.

The studies on radiography of the chest, which are summarized in this paper, relate primarily to the reliability of interpretation and not to its validity. In other words, interest is focused on the ability of the chest roentgenogram to detect abnormal shadows, rather than on whether a person with an abnormal shadow in his chest x-ray has the specific disease. Moreover, since the presence or absence of an abnormal shadow is revealed only by the impression which it makes on the mind of the person reading the film, the problem turns to the reliability of x-ray interpretation and is concerned primarily with the reproducibility of interpretation of chest roentgenograms.

As a consequence of the foregoing, the terms "positive" and "negative" have the following meaning: Positive: persons who have roentgenographic evidence of inflammatory disease. Negative: persons who do not have roentgenographic evidence of inflammatory disease.

For the purpose of these studies it does not matter what the clinical picture of the individual is. The latter fact can be established by the employment of several tests, of which the x-ray is only one, although a very important one. Our concern is to determine whether the data derived from the roentgenogram are reliable. This, of course, is the first requisite in order that its validity can be tested.

It may be important to indicate here that two factors contribute to the unreliability of x-ray interpretation, as indeed to that of most diagnostic tests. These are false positives and false negatives. A test which provides a high proportion of false positives is said to be of poor specificity; while one which misses many positives, and thus yields many false negatives, is said to be of poor sensitivity.

The studies on the reliability of interpretation of chest roentgenograms will be presented under the following general topics: (1) detection of lesions—presence or absence; (2) description and classification of pulmonary shadows; (3) evaluation of change—serial roentgenograms; (4) benefits of dual reading.

DETECTION OF LESIONS—PRESENCE OR ABSENCE

One of the more important activities in radiology relates to the separation of positives and negatives; that is, the identification of persons who possess roentgenographic evidence of disease, and those who are free from such evidence. This activity is performed by the radiologist in his daily practice, as well as in photofluorographic surveys which are conducted on a large scale. It is in the latter experience where the magnitude of the problem of unreliability of interpretation was first noted.

In a study aimed at comparing the reliability of different photofluorographic technics all the x-rays were interpreted independently by five different readers.[6] It became apparent that the multiple readings posed significant problems even in the simplest of activities, namely, that of separating the group into positives and negatives. Consider, for example, the results obtained from the interpretation by five physicians of the large 14 by 17 inch celluloid roentgenograms as shown in Table 1.

This table shows the distribution of 1,256 roentgenograms according to the number of positive readings which were obtained by five readers. For example, in 1,125 cases all the readings were negative. In twenty-seven cases all the five readings were that of positive; in forty-seven cases there were one positive and four negative readings, etc. It is obvious, first, that it is not possible to answer with any degree of conviction the simple question of how many positives there are in the group. Should we consider all the 131 individuals who had at least one positive reading, or possibly only the twenty-seven with five positive readings?

Indeed, how can we be sure that the 1,125 with five negative readings are negative? Had we subjected the films to another reading, it is very likely that some of them would have been called positive. In fact, a set of one hundred 14 by 17 inch x-rays, which when selected were thought to contain one-third positives, was interpreted independently twenty times. The more readings that were obtained, the smaller the group became in which all the readings were negative. At last count, after twenty interpretations, only sixteen of the set of 100 roentgenograms were called negative in all twenty readings. On the other hand, in only seven cases were all the twenty readings in agreement on positive.

These simple facts illustrate that observer errors which accompany the interpretation of roentgenograms for the presence or absence of a lesion are of disturbing magnitude. The variability is a result of two factors which should be studied separately: that of over-reading or false positives, and under-reading or false negatives. Estimates of the magnitude of these two factors may be obtained from a study of 1,807 photofluorograms (70 mm.) which were interpreted independently ten times.[7] It was possible to establish with reasonable certainty that the set contained thirty roentgenologically positive films; that is, on these thirty films there was unanimous opinion by seven expert radiologists and phthisiologists that they showed evidence of inflammatory disease requiring clinical study. In a similar way it was established that the set contained 1,760 roentgenologically negative films.* It was thus possible to determine for each reader how many of the thirty positive films he missed, and how many false positive diagnoses he made on the 1,760 negatives.

As a result of the ten interpretations of the photofluorograms it was found that on the average *a competent and experienced physician misses, in a single reading, as many as 32.2 per cent of the positive films, and provides false positive diagnoses on 1.7 per cent of the negative films.* These results are not limited to the 70 mm. photofluorograms. Similar findings were noted for other film sizes, including the 14 by 17 inch celluloid roentgenograms.

* There were in addition seventeen films in which the opinion of the special panel was divided. The corresponding photofluorograms were eliminated from the study.

These findings bring into focus one serious practical problem which results from observer error in chest radiography. When a photofluorographic survey is being conducted in a community or in a hospital and the films are interpreted by a competent radiologist or a chest specialist, approximately one-third of the persons whose photofluorograms contain evidence of inflammatory disease are being told that they are free from disease while over 1 per cent of the negatives are being told that their x-rays indicate possible disease. The seriousness of the problem for the former is obvious. The situation, however, is not unimportant for the latter group; they are being subjected to inconvenience, expense and psychologic trauma before they are satisfied that the original positive diagnosis was false.

TABLE 1*

DISTRIBUTION OF 14 BY 17 INCH ROENTGENOGRAMS ACCORDING TO NUMBER OF POSITIVE READINGS IN FIVE INDEPENDENT INTERPRETATIONS

Number of Positive Readings	No. of Films	Per cent of Films
0	1,125	89.6
1	47	3.7
2	23	1.8
3	17	1.4
4	17	1.4
5	27	2.1
Total	1,256	100.0

* From BIRKELO, C. C. et al. *J. A. M. A.*, 133: 359, 1947.[6]

Many people have the conviction that from a practical point of view the problem may not be as serious as the foregoing results indicate. It is argued that the positive films which are missed may not be the important ones, and that all clinically significant lesions are being detected by all competent readers. This point has not yet been entirely settled since it is difficult to obtain reliable information on the subsequent follow-up of persons whose lesions might not have been detected in a single read-

ing. The results of one study[8] are very suggestive, and indicate that clinically active lesions may be overlooked in a single reading and that the frequency with which false negative diagnoses are given on such lesions is no smaller than that for inactive lesions. The study, however, is based on only a small number of active lesions. It must be confirmed by more extensive investigations before the results can be accepted.

DESCRIPTION AND CLASSIFICATION OF PULMONARY SHADOWS

Much more serious discrepancy than that found in studies on detection of lesions was found in evaluating the reliability of describing and classifying roentgenographic shadows. The task, of course, is much more difficult, and the unreliability should have been expected. It is surprising, therefore, that until recently practitioners in this field were convinced that they were able to interpret a lesion not only for its probable significance at the moment but also as to its possible prognosis. In fact, a large segment of physicians practicing in this field still believe that they can do it.

As a result of the demonstration of the magnitude of unreliability in x-ray interpretation, a group of three radiologists—Drs. W. Edward Chamberlain, R. R. Newell and Leo Rigler—has undertaken to investigate the reliability of describing and classifying pulmonary lesions. These men attempted to develop more reliable methods for accomplishing this task because they realized that any significant, lasting progress and improvement in roentgenographic interpretation is dependent on the development of a reliable method of describing and classifying lesions.

The results of their investigations were extremely disappointing. They had tested nearly all methods of describing and classifying lesions now in common use. They had demonstrated, beyond a doubt, that it is not possible to determine the probable activity of a lesion from a single roentgenogram. When one radiologist calls a lesion active, a second, equally competent radiologist is likely to disagree with him in nearly 50 per cent of the cases. Nor is the description of a lesion in terms such as "hard," "fibrotic," "exudative," "productive," etc., any more discriminating. Disagreements as high as 55 per cent were noted in the words and symbols used by the radiologist in his daily practice of interpreting films.

It may be of interest to quote here from a recent paper reporting on the work of this group:[9]

"The present writers appear to have failed in this project of finding a reliable classification of the roentgenographic appearance or quality of a tuberculous pulmonary lesion. It is believed that reasonable degrees of tenacity and resourcefulness were used in the attempt. It was disappointing to find that many conferences and much practice, together and apart, failed to increase reliability and agreement to a useful degree.

"Analysis shows that the amount of agreement was statistically significant, i.e., that differences in structure of the shadows were really being perceived. Nevertheless, the agreement was quantitatively insufficient for the purpose envisaged, namely, validation of a classification by long-time clinical studies.

"The more subjective judgments of activity (intuitive) appeared to be about as reliable as description and classification of the objective appearance of the lesion on the film.

"Success in classification (diagnosis) seems not to be attained by instructing the reader to 'mark it only if you feel sure.' To do this results either in an increase in disagreement or merely in an overwhelming reduction in the number of useful diagnoses ventured. The percentages of agreement and disagreement depend on how broadly agreement is defined. But the more generous one's definition of agreement, the less sharp the classification and the less use it will have for clinical purposes.

"In discussing this research with others, radiologists and chest specialists, the writers find a general unwillingness to believe that descriptions of pulmonary lesions are as unreliable as were found in the present study. The present writers have become accustomed to this skepticism and believe that only those who have themselves made duplicate readings of a series of films can come to appreciate the hard fact of their own unreliability.

"Even yet the conviction survives that the qualitative appearance of a lesion as seen on a chest film must have clinical significance. The present investigators believe that further effort should be made to find ways to bring out in optimal degree all of the information that may actually be there."

EVALUATION OF CHANGE—SERIAL ROENTGENOGRAMS

Serial roentgenograms of the chest are utilized in case management for the purpose of assessing the course of disease in a patient with pulmonary disease. In the course of study of the patient considerable information becomes available in addition to data provided by the roentgenograms. The latter, however, are considered to provide the most reliable estimates of change in extent and character of the lesion. The main changes occurring in a pulmonary lesion are usually reflected in changes in its roentgenographic shadows. Serial roentgenograms have therefore been accepted with a great degree of confidence as objective tests of the progress of the disease and its activity. It is not uncommon that the evaluation of change as perceived by a comparison of serial chest x-ray films is relied upon almost exclusively in case management. The findings that the interpretation of serial roentgenograms are also grossly inconsistent were, therefore, even more unexpected than those relating to a single roentgenogram.

A comprehensive analysis of the reliability of interpretation of serial roentgenograms was conducted with the cooperation of six competent physicians—three radiologists and three phthisiologists.[10] They interpreted 150 pairs of 14 by 17 inch anteroposterior roentgenograms taken on patients with proved tuberculosis at three monthly intervals. Each physician classified the 150 pairs in only three groups: whether on the basis of a comparison of the first and second film there had been, in his judgment, a "change for the better," a "change for the worse," or that the lesion "remained substantially unchanged."

After a lapse of some time, and without knowledge of the results of the first interpretation, the same pairs of roentgenograms were reinterpreted by the same readers in the same manner. This provided a total of twelve independent interpretations on each pair. Since two readings were made by each physician, it was possible to study the consistency of each reader with himself (intra-individual), as well as to compare the interpretations of each with those of the other five physicians (inter-individual). The main findings of this study are shown in Table 11.

It may be seen that there was a total of 8,931 comparisons between individual readers. These are obtained in the following manner: For each film pair, four comparisons are available for each pair of readers. For example, the first reading of reader A can be compared to the first and second readings of reader B, and the second reading of A can similarly be compared to the two readings of B. Since there are fifteen ways of comparing the six readers against each other, a total of sixty comparisons of one-against-another is available for every pair of films. For the entire group of 150 film pairs a total of 60 multiplied by 150, or 9000 comparisons, is available.*

TABLE 11*

PERCENTAGE OF DISAGREEMENTS BETWEEN READERS (INTER-INDIVIDUAL) AND FOR AN INDIVIDUAL READER WITH HIMSELF (INTRA-INDIVIDUAL) IN INTERPRETING 150 FILM PAIRS

Comparisons	Inter-individual		Intra-individual	
	No.	Per cent	No.	Per cent
Disagreements	2,686	30.1	192	21.5
Agreements	6,245	69.9	701	78.5
Total	8,931	100.0	893	100.0

* From YERUSHALMY, J. et al. *Am. Rev. Tuberc.*, 64: 225, 1951.[10]

These comparisons can be either agreements, that is the two readers classified the pair in the same way, or they are in disagreement. In all there were 2,686 comparisons which were in disagreement. These represent 30.1 per cent of all the comparisons between readers (inter-individual). A similar method showed that there were 192 cases in which a reader disagreed with himself. These represent 21.5 per cent of all comparisons of a reader with himself (intra-individual). It can therefore be stated that *in judging a pair of x-ray films for evidence of progression, regression or stability of disease, two competent and experienced physicians are likely to disagree with each other in nearly one-third of the cases, and a single reader is likely to disagree with himself in about one-fifth of the film pairs.*

* There were not exactly 9,000 comparisons because occasionally a reader designated a film pair as of non-diagnostic quality. These comparisons were left out. The total number of usable comparisons was 8,931.

While the majority of disagreements were of a single degree, that is, where one reader called the pair "no change," while the other called it either "better" or "worse," instances of complete reversal from better to worse were not uncommon. In fact, as a result of this study it may be stated that when a reader compares a pair of roentgenograms and decides, on the basis of the comparison, that the lesion is getting better or worse, the chances are that in approximately 10 per cent of the cases another equally competent reader will use the opposite classification to describe the same pair; and the same reader is likely to reverse his original diagnosis completely in approximately 7 per cent of the readings of the same set of film pairs.

This demonstrated unreliability of interpretation of serial roentgenograms is, in many respects, more serious than the unreliability of interpreting single roentgenograms because of its wide use in the practice of chest diseases. Many an important clinical decision affecting the patient often rests on the interpretation of change as seen on two films taken at two periods of time. The revelation of the insecure foundation on which it sometimes rests serves to underscore the fact that the dynamic status of pulmonary lesions cannot be determined without many observations, in addition to the comparison of serial roentgenograms of the chest.

BENEFITS OF DUAL READING

The demonstration of unreliability of interpretation of single roentgenograms, and of serial chest x-rays, has stimulated investigations on the development of methods for reducing the undesirable effects of false diagnosis. One obvious method is that of submitting all roentgenograms to more than one interpretation. The tests have been confined primarily to the evaluation of dual reading of single roentgenograms in mass radiography. To a more limited extent, the method of dual reading has been investigated for serial x-rays and its application in clinical practice. It may be well to present the results separately.

Dual Reading of Single Photofluorograms. The procedure of dual reading in mass radiography involves the following steps: The set of photofluorograms is first interpreted by one reader who selects all the films which in his judgment show evidence of inflammatory disease requiring further clinical study. Later the same set is reinterpreted in the same way by the same or another reader, *without knowledge of the results of the first reading.* This procedure may be expected to reduce the number of false negatives, that is, the number of cases with radiographic evidence of disease which are interpreted as negative. The reason for this is that the missing of a positive lesion often is the result of an accidental oversight on the part of the reader. It may therefore be expected that the probability that the same lesion will be missed on two independent occasions will be greatly reduced.

However, the method of dual reading has also an undesirable feature: It increases the proportion of false positives, that is, cases in which negative photofluorograms are called positive. The importance of this feature cannot be minimized since it is a source of great inconvenience to the patient. Methods have therefore been sought which attempt to retain the benefits of dual reading without incurring its disadvantages.

The study of dual reading is based on the survey of 1,807 individuals, mentioned previously, in which there were thirty roentgenologically positive and 1,760 roentgenologically negative cases.[7] They were interpreted ten times by experienced and competent physicians. A measure of the unreliability of interpretation may be judged from the fact that none of the readers selected all the thirty positives. At most, a single reader detected twenty-two of the thirty, and it was as low as seventeen of the thirty for one reader. Similarly, the number of false positives varied with the readers from fifteen to forty-six. On the average, a reader selected 20.3 of the thirty positive films and missed nearly one-third of them; he gave false positive diagnoses for 29.7 of the 1,760 negative films.

The addition of a second reading detected on the average 3.3, or approximately one-third of the 9.7 positive photofluorograms missed by the original reader. However, the second reading added 27.8 additional false positives. Photofluorograms which were interpreted as positive in two independent readings had a high probability of being truly roentgenologically positive. This happened on the average in nineteen cases, and 17.1 of these proved to be truly positive.

On the basis of this study it may be stated that if a set of photofluorograms is submitted

to dual readings, a large number will be called negative on both readings and a small number will be called positive on the two independent interpretations. These films will have a high degree of reliability, and disposition of these cases can be accomplished with a great degree of confidence. The cases in which the two readings are in disagreement call for special treatment in order to reduce the disadvantages of false positives.

In the study referred to, these cases were submitted to a third interpretation by another reader and by a panel of readers. It was found that by accepting the verdict of this third interpretation as a basis for action it is possible to retain much of the benefit of dual reading and, at the same time, to eliminate many of the additional false positives which result from dual reading. The results of this study are shown in Table III, which presents the benefits and disadvantages of the various methods of dual reading. The figures have been extrapolated to represent a survey in which there are 100 positives among approximately 6,000 photofluorograms.

It may be seen that a single reader detects sixty-eight of the 100 truly positives and misses thirty-two. He bothers, unnecessarily, ninety-nine individuals; that is, he gives false positive diagnoses on 1.7 per cent of the truly negatives. When the films are submitted to dual reading, seventy-nine of the 100 positive films will be detected in one or the other of the readings. However, the number of false positives will increase to 192, or nearly twice as many as in a single interpretation. The two readings will *both* be positive in sixty-three instances, fifty-seven of which will represent truly positives. The table also shows what may be expected when the cases of disagreement are subjected to another interpretation, either by a panel of three or by a single reader.

It may be seen that either of the methods is effective. The method of choice seems to be

TABLE III*

COMPARISON OF SINGLE READING WITH DIFFERENT METHODS OF DUAL READING†

Method of Reading		Survey of 5,967 Persons Containing			
		100 Truly Positives		5,867 Truly Negatives	
				Falsely Diagnosed As Positive	
		No. of Truly Positives Detected	No. of Truly Positives Missed	No.	Per cent (c/5,867) × 100
		a	b	c	d
Single reader		68	32	99	1.7
Two readers (one *or* the other)		79	21	192	3.3
Two readers (*both* agreed)		57	43	6	0.1
Panel of three: two readers in agreement plus review of disagreements when the decision of the panel was	Positive by unanimous opinion	75	25	72	1.2
	Positive by at least one reader	78	22	107	1.8
"Panel" of one: two readers in agreement plus review of disagreements by a single reviewer	Average of five performers	74	26	83	1.4
	Average of two best performers	78	22	99	1.7

* From YERUSHALMY, J. et al. *Am. Rev. Tuberc.*, 61: 443, 1950.[7]

† Number of truly positives detected and number of truly negatives diagnosed falsely as positive in a *hypothetic* 70-ml. survey of a group of 5,967 persons. This is an extrapolation from a real group of 1,790 persons presenting 30 truly positive films to a group sufficiently large to present an even 100 truly positives (exclusive of questionable films).

that which utilizes a single reader for reviewing all films in which the two readings are in disagreement. In other words, all films which are diagnosed as positive in *both* readings are immediately referred for clinical study. The films with contradictory diagnoses are reviewed by a competent reader (with knowledge of the results of the previous readings). Only those which are considered positive on this third interpretation are referred for further clinical study. Such a procedure detects 30 per cent of the truly positives missed by a single reader without increasing the number of false positives.

Dual Reading of Serial Roentgenograms. An evaluation of the role of dual reading of serial roentgenograms[11] was made on the same material utilized in the study on serial roentgenograms previously mentioned.[10] This, it will be recalled, consisted of 150 film pairs taken on patients with proved tuberculosis at three monthly intervals.

For the purposes of evaluating the benefits and disadvantages of dual reading it was necessary to determine for each film pair the probable true situation with regard to change. This was accomplished by submitting the film pairs to a group of competent radiologists and phthisiologists for discussion and determination of probable true status. Only film pairs on which it was possible to obtain a unanimous decision by this group were used in this study. There were eight cases on which the group could not agree as to the probable true status. These were eliminated and the study was based on the remaining 142 film pairs. As a result of group discussion these 142 pairs were placed in the following groups: sixty-three as representing roentgenologic evidence for better, fifty-nine for no change and twenty for worse.

With this information about the probable true status of each pair it is possible to investigate the relative merits of single and dual reading in serial roentgenograms. It should be noted that such percentages of false diagnoses as were found represent understatements, since the eight pairs which were left out of the study are the most difficult. Even in this somewhat easier set of 142 film pairs, a single reader was found to be correct in his interpretations 80.8 per cent of the time, and to give a wrong diagnosis approximately one of five times.

When serial roentgenograms are interpreted by two readers, they may be considered as falling in two main groups: one in which the two readings are identical and the other in which the two interpretations conflict. The major findings of the study are that in the first group the correct diagnoses are attained 94.2 per cent of the time. In other words, *when two readers place a film pair in the same category, there is a very high probability that that category is the true one.*

For films in the second group, no definite action with regard to the film pair is possible since the interpretations are conflicting. These represent 29.7 per cent of film pairs. These may be submitted to a third interpretation, or it may be more desirable to consider them as *roentgenologically undetermined.*

The results of the study may be restated as follows: The major advantage of dual reading of serial roentgenograms is that it identifies approximately two-thirds of the pairs for which the diagnosis can be given with a great degree of confidence. These represent the two-thirds of the film pairs which will have identical diagnoses in the two interpretations.

The procedure of dual reading also identifies the remaining one-third as the problem pairs, that is, those with conflicting diagnoses. It is, of course, possible to proceed in this case as in the case of dual reading of single roentgenograms, and submit these to a third interpretation. There is one slight difference in that the third interpretation does not always agree with one of the previous two—it may produce the third diagnosis. When the third interpretation agrees with a previous one, that diagnosis will be the correct one in two-thirds and incorrect in about one-fifth of these questionable cases. In the remaining there will be no workable diagnosis since all three interpretations will be given in the three readings.

COMMENT

It is apparent from the foregoing that the interpretation of a chest roentgenogram is not as reliable as desired for the more exacting tasks of diagnosis and treatment. Although these studies have been conducted mainly on material relating to mass radiography, it is very likely that in clinical radiology the problem of observer error may also be serious. In fact, the study on serial roentgenograms came very close to simulating practical day-to-day activities in clinical radiology and phthisiology. The results of that study suggest that prob-

lems of similar magnitude may be expected in other phases of clinical radiology. It is therefore important to consider methods for reducing as much as possible the probabilities of false diagnosis in clinical practice.

The problem would not have been so acute if it were possible to determine beforehand which roentgenograms present difficult diagnostic problems. If it were possible to separate the easy from the difficult cases, then, at least on the former, diagnosis could be given with confidence. It has been shown,[11] however, that it is not possible to identify which roentgenograms are easy and which are difficult of diagnosis; "a reader was unable to agree with other readers or with himself as to which of the pairs of films were difficult." In fact, it often happens that disagreement is greater on films thought to be easy of diagnosis than on those which were initially considered to be difficult.

It is this inability to determine *a priori* which of the roentgenograms present difficult diagnostic problems which is so disturbing because the insecurity and doubt must now relate to *all roentgenograms*. The radiologist or chest specialist who expresses an opinion on *any roentgenogram* must be prepared to be contradicted by his colleagues a significant proportion of the time.

It is in this area of separating the easy from the difficult roentgenograms that the procedure of dual reading may be expected to make the greatest contribution in clinical radiography. When the roentgenograms are interpreted independently by two different readers, they are separated immediately into two groups: (1) those in which the two interpretations are identical and (2) those with conflicting diagnoses. For the first group the agreed upon diagnosis can be given with great confidence. The probability that the roentgenologic diagnosis is wrong on this group is very slight. The procedure thus salvages a relatively large proportion of roentgenograms from uncertain and doubtful diagnosis and action.

The procedure also identifies the second group as those difficult of diagnosis. With respect to these, the best action probably is to leave them for the moment as *roentgenologically indeterminate;* that is, to admit that on the evidence available roentgenography can contribute little to the diagnosis of these cases. This seems to be a small price to pay for the greater assurance and confidence in the roentgenographic diagnosis of the much larger group of roentgenograms.

It may be important to indicate that an essential feature of dual reading is that the two interpretations be accomplished *independently* without knowledge of the results of the other interpretation. Group consultation never attains the required degree of objectivity.

SUMMARY

Observer error in chest radiography is of such magnitude as to create special problems in diagnosis and treatment. A review of recent studies on the subject reveals the following:

1. In interpreting a set of photofluorograms for presence or absence of a lesion a competent and experienced physician misses, in a single reading, as many as 32.2 per cent of the positive films and provides false positive diagnosis on 1.7 per cent of the negative films.

2. Classification of pulmonary lesions on the basis of roentgenographic appearance is not very reliable. It is not possible to determine reliably the probable activity of a lesion from a single roentgenogram.

3. In judging a pair of serial roentgenograms for evidence of progression, regression or stability of disease, two competent and experienced physicians are likely to disagree with each other in nearly one-third of the cases, and a single reader is likely to disagree with himself in about one-fifth of the pairs.

4. The undesired effects of false diagnosis may be reduced considerably by the application of dual reading. In mass radiographic projects this procedure detects one-third of the lesions missed by a single reader.

5. It is suggested that dual reading may be useful in clinical radiology. The main contribution results from the fact that the procedure identifies about two-thirds of the roentgenograms for which the diagnosis can be given with confidence. The remaining may be considered as *roentgenologically indeterminate* until further evidence is obtained.

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The Clinical Differentiation between Cardiac and Pulmonary Diseases

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THE clinical differentiation between cardiac and pulmonary diseases, although very important, is often difficult because of certain basic facts. In the first place, it is not uncommon to find both heart and lungs coincidentally affected in the same individual, especially at older ages. A common example of this is the finding in old men who are both breathless, because of chronic bronchitis and pulmonary emphysema, and bothered by angina pectoris due to coronary heart disease; or their breathlessness may be in part due to emphysema and in part to weakness of the left ventricle secondary to calcareous aortic stenosis. Not infrequently it is difficult to calculate the relative responsibilities of heart disease and of pulmonary disease in the production of symptoms and signs. More will be said about that later, but perhaps the most significant point is to remember that both organs can be affected simultaneously.

It is also of great importance to recognize that disease of one organ, heart or lung, may be responsible for disease of the other. Thus serious chronic fibrosis of the lung, as in the case of silicosis or of pulmonary arterial obstruction from massive pulmonary embolism, acute or chronic, or from endarteritis obliterans, may produce acute or chronic cor pulmonale with its enlarged right ventricle. Similarly, severe mitral stenosis, left ventricular failure of long-standing, and constrictive pericarditis involving chiefly the left heart chambers can produce so much pulmonary hypertension that pulmonary arteriosclerosis follows. Indeed, a considerable degree of pulmonary arteriosclerosis secondary to these conditions may in turn have its own effect on the right ventricle producing some degree of the cor pulmonale.

Another important consideration is that in the presence of disease of one of the organs, heart or lungs, the onset or increase of disease of the other may aggravate symptoms and signs due to disease of the former without being the cause of that original disease. Thus coronary heart disease may be severely aggravated by pulmonary embolism, pneumonia, lung abscess or pleural effusion with exacerbation of angina pectoris, or even the precipitation of coronary thrombosis with or without myocardial infarction. Similarly, the disability due to chronic bronchitis with emphysema or to pulmonary embolism may be made much worse by the presence of mitral stenosis or left ventricular failure or acute coronary thrombosis. Also, it should be emphasized that now and then symptoms and signs of diseases of both organs, heart and lungs, may be precipitated or aggravated by diseases somewhere else in the body, such as acute cholecystitis or a cerebral vascular accident, which, however, do not themselves cause heart disease.

The final basic consideration is that neither heart disease nor pulmonary disease may be present to explain symptoms that are ordinarily attributed to either or both of these conditions. Physiologic factors or extrathoracic conditions may cause reactions in normal heart and lungs that can sometimes be misleading. One of the most common examples of this is that of neurocirculatory asthenia, the cause of which is not clear but which constitutes a definite entity comprising a group of symptoms, in particular dyspnea, often of the sighing variety,

chest pain more often precordial than elsewhere, palpitation and faintness.

SYMPTOMS

In the clinical differentiation of cardiac and pulmonary diseases it will be of interest and value to discuss symptoms that may be independently associated with either heart or lung disease. The most prominent of these symptoms which may cause confusion is that of *dyspnea*. Shortness of breath is one of the chief symptoms of heart disease but it is also one of the chief symptoms of lung disease. Until the end of the seventeenth century shortness of breath was ordinarily ascribed to lung disease. That was before the institution of postmortem examinations. Quite suddenly it was discovered that a person might die with severe dyspnea and have relatively normal lungs but a very large heart (Bonetus, 1679).

There are many pulmonary diseases that cause shortness of breath, both acute and chronic; they are largely of an infectious nature although happily such infections are becoming steadily rarer. Pneumonia, extensive tuberculosis, influenza, malignant disease, pleurisy with large effusions, pneumoconiosis and pulmonary embolism are the more important diseases of the lungs responsible for dyspnea. The two most important cardiac conditions causing dyspnea are: (1) more common, failure of the left ventricle resulting in congestion of the lungs; and (2) less often, mitral stenosis. It is generally quite easy to diagnose these two cardiac conditions and to differentiate them from pulmonary disease. Another important cause of dyspnea is the occurrence of a large pericardial effusion. Once in a while, as already stated, both heart disease and pulmonary disease are present in the same person and may both share the responsibility for dyspnea. In such a case in which left ventricular weakness is a possible factor it is wise to give digitalis as a therapeutic test; often there is a gratifying response with considerable decrease of the dyspnea.

A very important clue to exonerate the heart as a cause of dyspnea is x-ray evidence of its normal size. If there is no enlargement of the left ventricle and no enlargement of the left auricle, both of these conditions, that is, left ventricular failure and mitral stenosis, can be pretty clearly ruled out. Once in a great while the heart in general in mitral stenosis may be practically of normal size but invariably there will be some enlargement of the left auricle, which should be carefully looked for.

Cheyne-Stokes dyspnea, that is, alternating apnea and hyperpnea, is to be attributed to cerebral vascular insufficiency, no matter what the cause. Sometimes the heart is partly responsible for this because of an inadequate output of blood, but more often there is cerebral vascular disease or serious renal involvement.

Pain is the next symptom of importance in the clinical differentiation of cardiac and pulmonary diseases. Although there may be deep-seated pain or oppression in the lungs as in the case of some instances of malignant disease or pulmonary embolism, due in the latter case probably to dilatation of the pulmonary artery, pain, except for its involvement of the pleura, is not a common symptom of diseases of the lungs. Pleural pain is quite easily differentiated from cardiac pain except when there is pleuropericarditis. Such pain is aggravated by breathing in contrast to cardiac pain which is not. *Angina pectoris* and the *pain of coronary thrombosis* are too easily diagnostic to require discussion in this relationship. On the other hand, the heartache of neurocirculatory asthenia or pain in or superficial to the chest cage from trauma or bursitis, the discomfort of herpes zoster, and "cardiospasm" are of course to be differentiated from the pains due to either heart or lung disease; this is usually done with ease. Cardiospasm is the most common of all the disagreeable sensations induced substernally, usually with gaseous eructation, by the occurrence of spasm of the esophagus or upper end of the stomach.

Cough is rarely due to heart disease but is very commonly caused by pulmonary disease. There are, however, two cardiac conditions which may give rise to cough in rare cases. One of these is mitral stenosis which may result in such enlargement of the heart with displacement and pressure against the bronchi and trachea that cough is sometimes elicited. The other cardiac condition is congestive failure secondary to left ventricular weakness resulting from the strain of chronic hypertension, myocardial infarction or aortic valve disease. Usually it is easy to discover the presence of these cardiac factors. Now and then, of course, both heart and lung diseases may be causes of cough in the same patient.

Hoarseness, like cough, is preponderantly the

result of involvement of the respiratory tract. In very rare cases it is secondary to advanced mitral stenosis or pressure from an aneurysm of the thoracic aorta which may result in laryngeal paralysis.

Hemoptysis is also rarely due to heart disease. Like cough, it can result from severe mitral stenosis which is responsible for acute pulmonary edema and from congestive heart failure of high degree involving the lungs with bleeding therefrom. Pneumonia, pulmonary infarction and tuberculosis are the most common pulmonary causes of hemoptysis. *Pulmonary apoplexy*, which indicates a large hemorrhage, can occur with mitral stenosis but is more commonly the result of bleeding in pulmonary disease.

SIGNS

Fever may be found with either heart or lung disease; but since pulmonary infections are much more common than cardiac infections, fever is preponderantly a pulmonary sign. Although rheumatic fever involving the heart, subacute bacterial endocarditis, acute myocardial infarction and acute pericarditis are all associated with fever, such temperature elevation is usually of low degree and these conditions are as a rule easy to diagnose.

Tachycardia is common with both heart and pulmonary disease and therefore is in no way helpful in diagnosis except when the rate is very high (200, more or less), when some type of paroxysmal tachycardia becomes quite obvious. An important manifestation of pulmonary embolism is tachycardia out of all proportion to the amount of fever; in such a case the differentiation from heart disease is not always easy.

Tachypnea (increased respiratory rate) is infinitely more common with pulmonary disease than with heart disease. There is some increase, however, with congestive heart failure. One should remember too that breathing disorders, with or without tachypnea, are common in neurocirculatory asthenia without disease of either heart or lungs.

Cyanosis is much more common with pulmonary disease than with heart disease and yet the deepest cyanosis is found in congenital defects of the heart and great vessels, as, in particular, the tetralogy of Fallot. In such cases the differential diagnosis is easy.

Rales in the lungs are much more common in pulmonary disease than in heart disease and as such they are most frequently due to infection, asthma, emphysema or bronchitis. Dependent rales, especially at the extreme bases, are, however, fairly common in cases with failure of the left ventricle. As such they are a late sign of pulmonary congestion, the symptom of dyspnea itself, whether paroxysmal or not, being much earlier. Dry rales at the lung bases should be carefully distinguished from the moist rales of pulmonary edema. It should be stated here, however, that rales of asthmatic nature are not infrequently found in patients with acute pulmonary edema due to heart disease. In such cases the term *cardiac asthma* has been applied.

Dullness on percussion may be found at the lung bases, especially at the right, due to hydrothorax, in right heart failure and in chronic constrictive pericarditis; but except for these conditions which are usually diagnosed with relative ease, dullness to percussion is a sign of pulmonary disease. One important clue is that if dullness, with or without rales, is found at the left lung base and not at the right, the cause thereof should be sought in the lungs (for example, pulmonary infarction or left-sided pleuritis) and not in the heart except in rare cases where the left hydrothorax of congestive heart failure may be associated with obliteration of the right pleural cavity.

A *friction rub* heard over the chest is almost invariably secondary to acute pleuritis. However, it may be heard over the heart itself due to pericarditis. When pericarditis is attended by pleuritis, the term pleuropericarditis is applied.

The presence of loud *heart murmurs* indicates the presence of disease of the heart or great vessels, but frequently such disease is not responsible for symptoms or other signs. Many patients with valvular heart disease live long lives free of symptoms when there is only relatively slight deformity of mitral or aortic valve, while some of the most serious cardiac patients with heart failure have very little in the way of murmurs to be heard. This is particularly true of patients who have serious coronary heart disease even with angina pectoris decubitus or acute myocardial infarction.

Heart sounds are more important than heart murmurs. *Diastolic gallop rhythm* indicates dilatation of the left ventricle when maximal at the apex and dilatation of the right ventricle

when located at the lower end of the sternum. It should always be regarded as an important clue to the presence of serious heart disease. Accentuation of the pulmonary second sound is, however, an occasional finding in pulmonary disease, as in instances of extensive pulmonary fibrosis, massive pulmonary embolism or pulmonary endarteritis obliterans with increased pulmonary arterial pressure. Accentuation of the pulmonary second sound is, of course, also a common finding in cases with mitral stenosis and left ventricular failure. Therefore, as a clue, it must be judged very carefully.

X-ray evidence is extremely helpful although often only in a supplementary way. The *size of the heart* can be best determined, of course, in this way. The smaller the heart, the less likelihood of heart disease or that the heart is responsible for such a symptom as dyspnea or cough. Abnormalities of the great vessels are determined with exactness only by x-ray study, and many times it is only the x-ray film that reveals malignancy of the lung or the scar of a pulmonary infarct. Calcification of the pericardium is an important clue to chronic constrictive pericarditis. Pneumothorax and pleural and pericardial effusions are best determined by this technic. It is important in fluoroscopy of the heart to make observations from different angles, that is, in the oblique, lateral and postero-anterior positions.

The *electrocardiogram* is generally normal in the presence of pulmonary disease. Rarely extensive involvement of the lungs, acute or chronic, can alter the electrocardiogram as in the case of the rather typical acute cor pulmonale secondary to massive pulmonary embolism. In the acute cor pulmonale, the electrocardiographic pattern is that of the appearance or accentuation of S waves in lead I, Q waves in lead III, and inversion of the T waves in leads III, aVF, V_2 and V_3, and sometimes in lead II. To be sure, the electrocardiogram may be normal also in serious heart disease, for example, in coronary heart disease between attacks of angina pectoris, but advanced heart disease sufficient to cause dyspnea, cough, hoarseness and hemoptysis can be considered to produce practically always an abnormal electrocardiogram.

CONCLUSION

The clinical differentiation of cardiac and pulmonary disease is usually easy. Dyspnea, cough, hoarseness, hemoptysis, fever, tachypnea, cyanosis, rales and percussion dullness are more commonly found with lung than with heart disease although there are many exceptions. The symptoms and signs more commonly found in heart disease include pain, tachycardia, heart murmurs and abnormal heart sounds. To supplement the analysis of symptoms and signs, x-ray and electrocardiographic studies are invaluable and sometimes afford the conclusive clues.

The Effect of Chronic Pulmonary Disease on the Heart

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As far back as the eighteenth century the medical profession was aware of the fact that chronic lung disease could ultimately influence cardiac function.[1] The frequency of such occurrence and the degree of involvement continued to be a matter of controversy for many years thereafter. In the past two decades, however, renewed interest in this field has succeeded in accumulating a mass of evidence which has established beyond any doubt the fact that long-standing disease of the pulmonary tissue can and does affect the heart both anatomically and physiologically. It does so in a characteristic manner and to such an extent that it has come to be known by a special connotation, i.e., cor pulmonale or pulmonary heart disease.

Strictly speaking pulmonary heart disease or cor pulmonale are terms that should be applied to hypertrophy of the right ventricle, with or without failure, which results from diseases of the lungs, pulmonary vascular tree or thoracic cage. In a broader sense they are also being employed by some to include the right ventricular hypertrophy due to (1) congenital heart malformations of long duration in which there is a left-to-right shunt of large magnitude, and (2) mitral stenosis, with left ventricular failure.[2] The latter concept is misleading to the clinician, despite the fact that an increased resistance to blood flow through the precapillary portion of the lungs also exists in these primary cardiac conditions. For the purpose of clarification and in order to obviate any confusion, cor pulmonale is herewith defined as that type of heart disease in which right ventricular hypertrophy results solely from diseases of the lungs, pulmonary vessels or thoracic cage.

The etiology of pulmonary heart disease is manifold, as has been shown by the numerous studies of postmortem material, and its incidence varies with the area from which these reports emanate and the enthusiasm of the writer. Generally speaking, however, at the present time, it is much more common than heretofore, and all are agreed that it occurs more frequently in males than females, in a ratio of more than four to one, particularly in the older age group from fifty to seventy years. The causes of cor pulmonale have been well tabulated by McKeown[3] in England and by Spain and Handler[4] in this country, and to the latter series the present author has added a few cases either encountered personally or found in the more recent literature. (Tables I and II.) From Table II it can readily be seen that in the third group, which concerns us most, consisting of diseases of the lungs in which there are anatomic alterations of the pulmonary parenchyma, pulmonary emphysema is the common denominator. It is this underlying condition, with its disturbed pulmonary physiology, that is responsible for the production of increased tension in the pul-

TABLE I*
INCIDENCE OF RIGHT VENTRICULAR HYPERTROPHY IN 6,770 NECROPSIES

	Causes of Death		
	Incidence	Right Heart Failure	Others
Emphysema	39/101	20	19
Bronchiectasis	17/80	6	11
Asthma	14/24	9	5
Tuberculosis	7/92	3	4
Carnification	5/42	3	2
Embolism	5/103	4	1
Arteritis	4	4	0
Unknown cause	4	2	2
Primary carcinoma	3	0	3
Kyphoscliosis	3	2	1
Secondary carcinoma	2	1	1
Chronic cystic disease	2	1	1
Fibrosis	2	0	2
Organized int. pneumonia	2	1	1
Asbestosis	1	0	1
Hemosiderosis	1	1	0
Total	111	57	54

* Taken from McKeown.[3]

monary circuit and ultimate right ventricular hypertrophy.

The manner in which emphysema produces this effect is by no means a settled question, and in order to explain the pathogenesis many factors have been considered. These include

TABLE II

I. Anatomic alterations of the thoracic cage
   A. Kyphoscoliosis
   B. Thoracoplasty
II. Anatomic alterations of the pulmonary vascular system
   A. Main pulmonary arteries
      1. Intrinsic disease of the large pulmonary arteries, such as gummatous or cicatric pulmonary arteries
      2. Pressure on the large pulmonary vessels such as aneurysm arising from the base of the aorta
   B. Pulmonary arterioles
      1. Primary pulmonary arteriosclerosis: endarteritis obliterans (Ayerza's disease)
      2. Schistosomiasis of the pulmonary vessels
      3. Polyarteritis
      4. Lupus erythematosis
      5. Sickle cell anemia
      6. Recurrent pulmonary embolism
      7. Thrombosis of the pulmonary artery
III. Anatomic alterations of the pulmonary parenchyma
   A. Primary pulmonary emphysema with or without fibrosis
   B. Primary pulmonary disease with secondary emphysema and fibrosis
      1. Pulmonary tuberculosis
      2. Pneumoconiosis
         (a) Chronic silicosis
         (b) Anthracosis
      3. Bronchiectasis
      4. Bronchial asthma
      5. Acute interstitial fibrosis
      6. Multiple cysts of the lungs
   C. Systemic disease with secondary pulmonary parenchymal involvement
      1. Sarcoidosis
      2. Scleroderma

(1) anoxia, (2) anatomic obliteration of the pulmonary vascular bed, (3) retention of carbon dioxide with subsequent respiratory acidosis, (4) pulmonary vascular sclerosis, (5) vascular shunts between the systemic and pulmonary circulation, (6) overfilling of the heart, (7) polycythemia, (8) compression of the capillaries by the increased intra-alveolar pressure occurring during the respiratory cycle, and (9) diffuse fibrosis of the lungs. There is no doubt that many of these exist at one time or other during the course of the disease, and very likely all contribute in some degree to the production of pulmonary hypertension. From work recently reported,[5] however, it appears that the increased pressure in the pulmonary circuit is most probably due in the main to a combination of anoxia and anatomic obliteration of the pulmonary vascular bed, and that the others play a secondary role. If the foregoing is true—and it can hardly be challenged—then the frequently posed question why all cases of emphysema do not result in cor pulmonale still awaits an answer. It is possible that occupational, constitutional, endocrine and neurogenic components may play a significant part in determining who may or may not develop this disease. It must be remembered, however, that any case of obstructive emphysema regardless of its underlying cause is potentially able in the proper setting to develop the required pathologic stimulus which will lead eventually to an increased tension in the pulmonary circuit and to right ventricular enlargement.

Formerly cor pulmonale was recognized purely on clinical grounds or at autopsy, but at present, with the newer technics of cardiac catheterization at our disposal, this type of heart disease can be diagnosed long before overt signs of right ventricular failure present themselves. With these methods permitting direct measurement of the pressures within the pulmonary artery and right ventricle, a definite set of values has been obtained for normal human beings. (Table III.) In most cases of pulmonary emphysema, numerous workers employing the cardiac catheterization approach have demonstrated a distinct elevation of the pressures within these cavities. Bloomfield et al.[6] in 1946 reported an increase in the systolic pressure within the right ventricle in four of six patients with chronic pulmonary emphysema. Borden and his coworkers[7] a few years later showed that in all their twenty-four cases of chronic diffuse pulmonary emphysema the pulmonary diastolic pressure was distinctly elevated, and in the majority of their patients the pulmonary systolic pressure was also above normal. In addition, these authors demonstrated that there was no correlation between the severity of the emphysema, as estimated by the ratio of residual air to total lung volume, and the elevation of the pulmonary arterial pressure. In their group it was also noted that the pulmonary tension was much higher in those who recovered from right heart failure than in those who were never in failure. Harvey et al.[5] in 1951 studied

both pulmonary and cardiac function in forty-eight cases of chronic pulmonary disease, of which twenty-four were diagnosed as chronic pulmonary emphysema; eight patients were considered as suffering from silicosis and emphysema; ten were labeled instances of diffusion fibrosis in whom the physiopathologic pattern was characterized by interference of oxygen diffusion across the alveolocapillary membrane; and four were assigned to a miscellaneous group, of whom two apparently presented multiple embolization into the pulmonary arterial tree and two primary pulmonary vascular disease. These writers found that the degree of pulmonary hypertension and increased pressure in the right ventricle depended predominantly on the degree of oxygen unsaturation or anoxia and on the extent of the anatomic alterations in the pulmonary vascular bed produced by the disease process itself. They also demonstrated a greater pulmonary hypertension in patients with cor pulmonale while in congestive failure than when in a state of compensation. Many such patients presented a reversibility of their congestive failure, with long periods of remission, thus indicating a more hopeful prognosis than had heretofore been predicted in the congestive phase of cor pulmonale. Furthermore, the authors demonstrated an elevated pressure in the pulmonary artery and right ventricle in many who had shown no x-ray evidence of any enlargement of these chambers nor electrocardiographic abnormalities concomitant with right ventricular hypertrophy. In re-evaluating the cardiac output they found it to be either elevated, normal or low, depending upon the degree and type of the underlying pulmonary involvement. In chronic pulmonary emphysema, with marked anoxia and hypervolemia, they observed a high output and believed the increased blood volume to be responsible. A similar finding was also evident in patients with diffusion fibrosis without hypervolemia, and in such instances the high output was ascribed to the continuous activity of the disease rather than to a change in blood volume, which did not exist. In the silicotic group in which anoxia did not play an important role in the production of increased pulmonary tension but in which the predominant etiology was the anatomic obliteration of the vascular bed, the cardiac output was either low or normal. In the majority of instances of cor pulmonale the cardiac output is high, and in a few cases it may even be normal or low. This supports the work of previous observers and also indicates that since pulmonary emphysema is not a static disease the findings of one investigator may be entirely different from those of another, simply because the determinations were obtained during different phases of the disease in the same patient or at various stages in different patients.

TABLE III
NORMAL VALUES FOR PULMONARY ARTERIAL AND RIGHT VENTRICULAR PRESSURE

Reference	No. of Subjects	Right Ventricular Systolic (mm. Hg)		Pulmonary Arterial Diastolic (mm. Hg)	
		Average	Range	Average	Range
Bloomfield, R. A. et al. *J. Clin. Investigation*, 25: 639, 1946	14	25	18–30	..	....
Cournand, A. *Bull. New York Acad. Med.*, 23: 27, 1947	4	25	.....	8	....
Dexter, L. et al. *J. Clin. Investigation*, 26: 554, 1947	3	26	20–32	10	8–12
Motley, H. L. et al. *Am. J. Physiol.*, 150: 315, 1947	5	22	.....	6	....
Riley, R. L. et al. *Am. J. Physiol.*, 152: 372, 1948	3	20	.....	9	....
Borden, C. W. *Minnesota Med.*, 31: 1218, 1948	12	20.1	11–26	8.8	6–11

These physiologic observations noted by means of cardiac catheterization offer absolute proof that the heart is definitely involved in chronic pulmonary diseases. The fact that increased tension in the pulmonary artery and right ventricle can be demonstrated by this method long before overt signs of cor pulmonale appear has led many to believe that the only confirmatory method of diagnosing cor pulmonale antemortem is by means of this technic. Such a procedure, however, is far from a simple one either for the patient or for the physician. It is highly technical, requires special training and is not completely without danger. Fortunately, it is not the only method available. There is a distinct clinical picture, classic radiologic findings and characteristic electrocardiographic alterations that are of great assistance in the recognition of this type of heart disease.

The clinical syndrome of cor pulmonale may be divided into two major phases: an early pulmonary phase, in which the manifestations of the underlying pulmonary disease predominate, and the later cardiac stage characterized by the disturbances produced directly by the hypertrophy of the right ventricle and the increased tension in the lesser circulation.[8] The signs and symptoms of the pulmonary phase are: (1) cough, (2) cyanosis, (3) dyspnea, (4) clubbing of the fingers, (5) diminished expansion of the chest and an increase in its anteroposterior diameter, (6) fixation of the diaphragm and (7) polycythemia. The outstanding features of the second stage are: (1) engorged neck veins, (2) enlarged and tender liver, (3) generalized edema and (4) increased venous pressure. The transition from one phase to the other is extremely difficult to detect since cough, cyanosis and dyspnea, the preliminary signs of heart failure, are also indicative of the underlying pulmonary disease. However, an increase in the intensity of these findings or the appearance of orthopnea suggests the onset of right heart strain. It is well known that patients with emphysema breathe more comfortably lying down, whereas those with cardiac dyspnea are relieved by sitting upright. A positive hepatojugular reflux elicited by pressure over the right upper quadrant long before hepatic enlargement is felt is another early indication of cardiac failure in this type of heart disease. Cardiac hypertrophy cannot be detected by the usual means of physical examination, since the underlying emphysema interferes with the percussion note obtained. Regular sinus rhythm and normal blood pressure are the usual occurrence in chronic cor pulmonale, but occasionally an ectopic rhythm may be heard. Accentuation of the second pulmonic sound is a constant feature and this, in addition to the systolic murmur frequently audible over the pulmonic area, suggests the existence of increased intrapulmonary tension. In the compensated stage of this disease, before overt signs of failure appear, these two later findings plus an increase in cyanosis and the development of polycythemia are often the only manifestations of cardiac involvement.

Various studies of circulatory function have been performed by Oppenheimer and Hitzig,[9] who have shown the findings to be normal in uncomplicated pulmonary disease. In the early stages of pulmonary heart disease associated with right ventricular enlargement with compensation they are also normal. But when myocardial insufficiency sets in, these measurements become abnormal. Incipient right heart failure is characterized by the presence of a normal initial venous pressure and a varying rise in this pressure during compression of the right upper quadrant of the abdomen. The arm-to-lung circulation (ether) time may or may not be prolonged, and the lung-to-tongue circulation time (saccharin time minus ether time) is normal. In frank isolated right heart failure, however, there is a high initial venous pressure, with considerable rise upon right upper quadrant compression, a prolonged arm-to-lung time, and a relatively normal lung-to-tongue time. In mild cor pulmonale the circulating blood volume may be normal, but in severe cases with arterial anoxia and polycythemia it is increased and indicates decompensation.

Another link in the chain of evidence in favor of the clinical diagnosis of cor pulmonale is the characteristic cardiac silhouette seen roentgenographically, indicating hypertrophy of the right ventricle and dilatation of the pulmonary artery. In 1923 Dietlen[10] summarized the significant x-ray appearances of the heart in emphysema. He noted cardiac enlargement transversely to the right; prominence of the inferior right border, which is separated from the right auricle above by a groove; prominence of the pulmonary arch, with forceful pulsation there and at the lower right cardiac border; and elongation of the outline of the right ventricle in the lateral views. These observations were subsequently confirmed by many other workers. Parkinson and Hoyle,[11] in an excellent clinical and radiographic study of the heart in eighty patients with advanced emphysema, noted that changes in the root and larger branches of the pulmonary artery were the most frequent x-ray signs of right heart involvement. This finding was rarely demonstrable in the frontal view but was best visualized in the right oblique position. In the left oblique view the right ventricle could be detected only in a small proportion of cases. Rigler and Hallock[12] and Gelfand[13] also emphasized the need of all four standard positions, particularly the oblique, to demonstrate enlargement of the right ventricle and pulmonary artery in cases of pulmonary emphysema. Robb

and Steinberg[14] demonstrated by contrast angiocardiography an enlargement of the right ventricle and pulmonary artery in a case of pulmonary heart disease. Employing the same technic Sussman, Steinberg and Grishman[15] obtained similar results in twenty-four of twenty-eight cases of emphysema, thus indicating a high percentage of cardiac involvement in chronic emphysema. It is now generally agreed that the first x-ray sign of right cardiac enlargement is prominence of the pulmonary arch, i.e., the middle arch on the left cardiac border, forming the outflow tract. The hypertrophy progressively continues and presents itself later as an enlargement of the lower part of the right ventricle, the inflow tract. Because of these specific radiographic characteristics of the heart in cor pulmonale, it is frequently stated that next to cardiac catheterization the most accurate method of diagnosing cor pulmonale is the x-ray.

The electrocardiograph is an extremely useful tool for the detection of right ventricular hypertrophy, and thus in cor pulmonale, in which enlargement of the right ventricle is an outstanding feature, this modality should be of considerable value. While it is agreed that in the early stages of the disease, when the pulmonary resistance is not three times the normal, the changes on the electrocardiogram may be minimal, nevertheless an acquaintance with the electrocardiographic patterns which suggest right heart strain will prove very rewarding.

The earlier writers reported the following changes in emphysema and cor pulmonale: (1) right axis deviation, (2) RST depression, with inverted T waves in leads II and III, (3) deep S waves in all standard limb leads, and (4) P wave abnormalities consisting of tall and notched P in leads II and III. These alterations are not specific for right ventricular enlargement, for they may occur in normal as well as in vertical hearts with left ventricular hypertrophy. The introduction of multiple unipolar precordial and extremity leads, however, have added additional information permitting of a more accurate interpretation of right ventricular hypertrophy. Normally, leads V_1 and V_2 yield QRS complexes of the rS type, and V_4, V_5 and V_6, from the left side of the precordium, yield complexes consisting of a small q and tall R, with or without a small s wave. On the average, the peak of R is about 0.02 second earlier when the precordial lead is over the right ventricle than when over the left. In right ventricular hypertrophy, however, Wilson and his associates,[16] Goldberger,[17] and Myers[18] have shown that the reverse is true. From the right side of the precordium, V_1 and V_2, the QRS complex is chiefly an R wave with an occasional antecedent small q wave, and the s wave is either absent or relatively small. The T wave in these leads is characteristically inverted. From the left side of the precordium the r wave is small and the S wave prominent, with an upright T wave. There is a prolonged time interval between the beginning of the QRS complex and the onset of the intrinsicoid deflection in V_1, generally between 0.03 to 0.05 second, which is greater than is seen in V_5 and V_6.

An additional precordial lead V_3R, in which the exploring electrode is placed on the right chest at a point corresponding to V_3 position on the left chest, has been employed by Myers[18] and his group as well as by Kossman and his associates[19] in some cases of suspicious right ventricular hypertrophy not confirmed by the other precordial leads. In such instances it yielded a small q, a tall R and an inverted T wave in contrast to a small r and deep S normally obtained. An alteration in the unipolar limb lead VR, in which there is a tall R preceeded by a small q, is an additional electrocardiographic pattern indicative of right ventricular enlargement. The final pattern that may be seen in this type of heart disease is right bundle branch block either of the incomplete or complete variety. In the former there is a double peaking of the R wave in V_1 and a relatively broad S wave in V_6, with the duration of the QRS for .11 second or less. In the latter the total duration of the QRS is 0.12 second or longer, the peak of the final R wave in lead V_1 is later in time than the peak of the R wave in V_5 and the R waves in the leads from the right side of the precordium are more prominent, coarsely notched and double-peaked, without any Q waves preceding them. Demonstration of any of these aforementioned electrocardiographic deviations furnishes conclusive evidence of right-sided myocardial involvement.

Thus it is apparent from the foregoing discussion that chronic diseases of the lung—more commonly chronic pulmonary emphysema and pulmonary fibrosis, either individually or together, as may sometimes occur—produce

increased tension in the pulmonary artery and right ventricle, with ultimate hypertrophy of the right heart. Although previously this hypertension was suspected by indirect means, at present it can be accurately measured by cardiac catheterization. Its clinical counterpart is chronic cor pulmonale, and this syndrome can now be more frequently and accurately recognized on the basis of the following criteria: (1) the existence of chronic lung disease; (2) the absence of any other cardiac disease; (3) the development of an increase in the dyspnea or cyanosis already present; (4) the appearance of orthopnea; (5) accentuation of the second pulmonic sound, with or without a murmur over the pulmonic area; (6) a positive hepatojugular reflux; (7) radiographic demonstration of cardiac enlargement; and (8) an electrocardiographic pattern of right ventricular hypertrophy.

Successful therapy of cor pulmonale depends upon a proper understanding of the physiopathologic factors responsible for its development. In pulmonary emphysema, when obstruction due to bronchospasm and uneven distribution of air in the alveoli are the fundamental disturbances, aërosolized bronchodilators, oxygen and antibiotics are the most powerful weapons to bring relief. When hypercapnia develops in association with anoxia, or when the two are present concomitantly, Harvey et al.[20] suggest the use of a mechanical means of maintaining adequate alveolar ventilation while oxygen is being supplied. They believe that treatment with these artificial respirators should be systematized and given over a long period of time. When frank signs of congestive heart failure appear, they recommend in addition to digitalis, low-salt diet and diuretics, judicious phlebotomy to overcome the existing polycythemia. The beneficial effect of digitalis in this type of heart disease is questioned by some, since most of these patients have a high cardiac output.

In pulmonary fibrosis the primary difficulty is an interference with the oxygen diffusion along the pulmonary alveolar capillary membrane, and therapy here consists of the administration of oxygen by the usual clinical means, the giving of antibiotics and prescription of marked limitation of activity. When the fibrosis is due to a granuloma, cortisone and corticotropin (ACTH) have been suggested in an attempt to limit the cellular proliferation responsible for the fibrosis. Usually most of the patients in this group die from pulmonary insufficiency long before signs of right heart failure develop; but when the latter do appear, the treatment is the same as for all others in congestive failure.

Early diagnosis and correct understanding of the altered physiology of cor pulmonale will result in proper therapy which will prolong life in this crippling disease.

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Pulmonary Diseases Secondary to Heart Diseases

DIAGNOSIS AND TREATMENT

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PULMONARY complications are a frequent occurrence during the course of many heart diseases and are of vital concern to the thoracic surgeon as well as to the internist and chest specialist. Our rapidly expanding knowledge in both fields makes it imperative to establish the correct diagnosis if treatment is to be effective. Several congenital cardiac defects, acute and chronic inflammations of the heart and aorta, degenerative lesions of the coronary arteries and aorta and primary neoplasms of the heart are capable of producing a variety of pulmonary complications.

CONGENITAL CARDIAC LESIONS

Interest in this field has been reawakened since it is now possible to correct a number of congenital cardiovascular lesions by surgical means. These include patent ductus arteriosus, coarctation, tetralogy of Fallot, "vascular ring" anomalies, aberrant subclavian artery, septal defects, pulmonary stenosis and various transpositions.

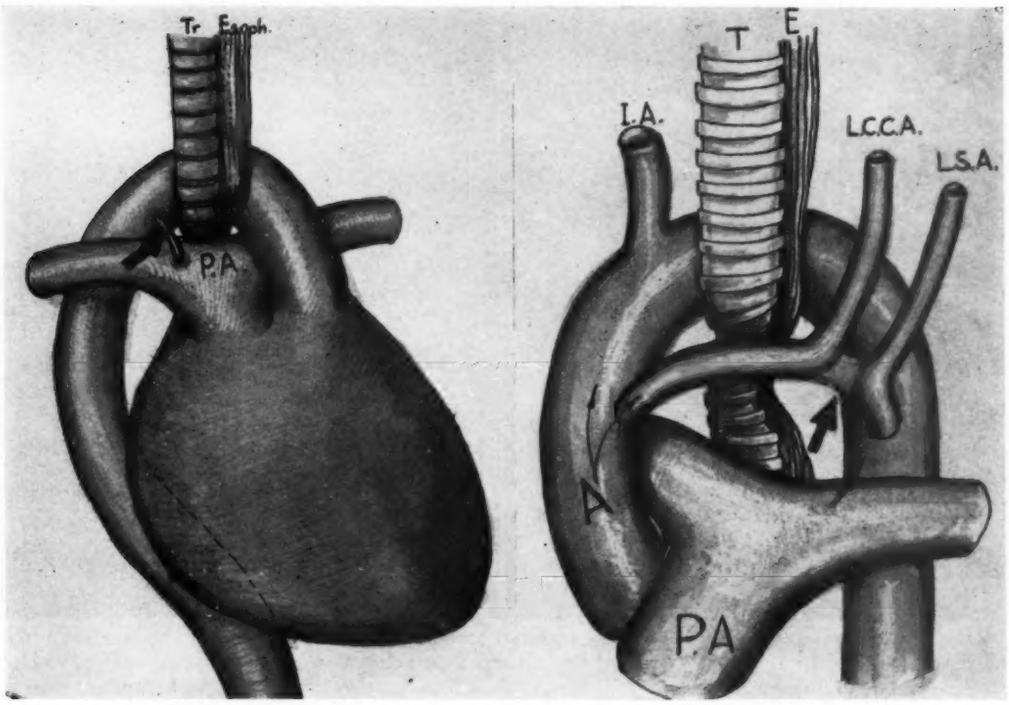
The only congenital vascular lesions which directly affect the trachea or bronchi by compression are the vascular ring anomalies.[1] Other defects, such as tetralogy of Fallot, produce dyspnea, cyanosis, clubbing, etc., but these are due to lack of proper oxygenation of blood because of the existence of abnormal shunts. However, all infants with cyanosis or dyspnea do not have congenital heart disease. A large diaphragmatic hernia, congenital air cyst, lung anomaly or pulmonary hemorrhage may simulate the signs and symptoms of congenital heart disease. In addition to insufficient pulmonary blood flow and congestive failure induced by some congenital lesions, subacute bacterial infections may result in embolic infarctions, multiple abscesses and bronchopneumonia.

Right Aortic Arch. This congenital anomaly may sometimes form a vascular ring by the constricting effect of a patent ductus arteriosus or ligamentum arteriosus. (Fig. 1.) It produces symptoms in the newborn by pressure on the right upper lobe bronchus thus producing atelectasis, obstructive emphysema or recurrent infections (trabeobronchitis or pneumonitis). It may also cause the pulmonary artery to compress the anterior surface of the trachea. Symptoms may be initiated later in life owing to traction caused by elongation and posterior displacement of the arteriosclerotic aorta. Pulmonary symptoms include dyspnea, cyanosis, cough and chest pain. Head retraction and stridor may occur in infants. X-ray studies of the barium-filled esophagus reveal an indentation at the level of the third intervertebral space.[2] Lipiodol studies in the lateral position delineate anterior tracheal compression just above the carina. Angiocardiography (7 second film) usually reveals the exact location of the vascular deformity.

When the obstruction produces symptoms, the ligamentum arteriosus is divided, allowing the pulmonary artery to fall forward.[3]

Double Aortic Arch. This anomaly occurs when both fourth branchial arteries persist. The left (anterior) arch is usually much smaller than the right. The vascular ring produces encroachment upon the trachea and esophagus, resulting in symptoms and diagnostic studies similar to those listed under the right aortic arch. Complete relief is afforded by the ligation and extirpation of the left (anterior) portion of the double arch. (Fig. 1.)

Pulmonary Stenosis. Pulmonary tuberculosis has been found to occur with greater frequency in the presence of several congenital heart conditions. This is especially true of pulmonary stenosis and tetralogy of Fallot. Abbott[4] found an incidence of 36 per cent and attributed this to the insufficient pulmonary blood flow. This explanation appears likely in view of the fact that tuberculosis seldom occurs in the chronically engorged lungs of



Right Aortic Arch Double Aortic Arch

FIG. 1. Vascular ring anomalies.

patients with mitral stenosis. Superimposed subacute bacterial infections with pulmonary embolization may also occur. This results in infarction, pneumonitis or lung abscess.

The Blalock shunt operation has been employed with success. A direct attack on the stenosing tissue by incision or punch operation produces equally satisfactory results in other cases, especially in those with an infundibulum.

Patent Ductus Arteriosus. Ordinarily the higher pressure in the aorta allows a return flow to the pulmonary artery through this abnormal communication. Pulmonary congestion may occur eventually if the shunt is of considerable size. The most frequent complications are congestive heart failure and subacute bacterial endocarditis. The latter results in embolic infarctions of the lung. Multiple small abscesses or patchy pneumonitis may ensue. Ligation and section of the ductus and the use of antibiotics are producing remarkable cures. The operation is contraindicated if evidences of pulmonary hypertension appear during the course of this disease.

ACUTE RHEUMATIC FEVER

Rheumatic Pneumonia. Rheumatic pneumonia is a rare but integral phase of acute rheumatic fever since the collagen tissue and its ground substance may be affected in any part of the body. An incidence of pulmonary involvement has been reported by numerous observers as varying from 2 to 15 per cent of all cases. The occurrence would be noted in a much larger percentage if all patients with acute rheumatic fever had chest x-rays at frequent intervals but especially at the height of an attack of acute rheumatic fever. The pathologic changes consist essentially of irregularly scattered areas of hemorrhagic consolidation. Cough and sputum are not prominent features. The diagnosis rests on finding[5] signs of transitory or migratory pulmonary exudates. This is demonstrable on serial x-ray studies. (Fig. 2.) Part of one lobe may be involved or the inflammatory process may extend to all the lobes. The lesions clear rapidly following the use of ACTH or cortisone, but this is difficult to evaluate because of the evanescent character of the lesions.

Pleurisy. Pleurisy is probably another manifestation of inflammation of the subendothelial connective tissue. Although acute fibrinous or serofibrinous pleuritis is recognized clinically in only 5 to 15 per cent of all cases of acute rheumatic fever, it is found in half of the cases that

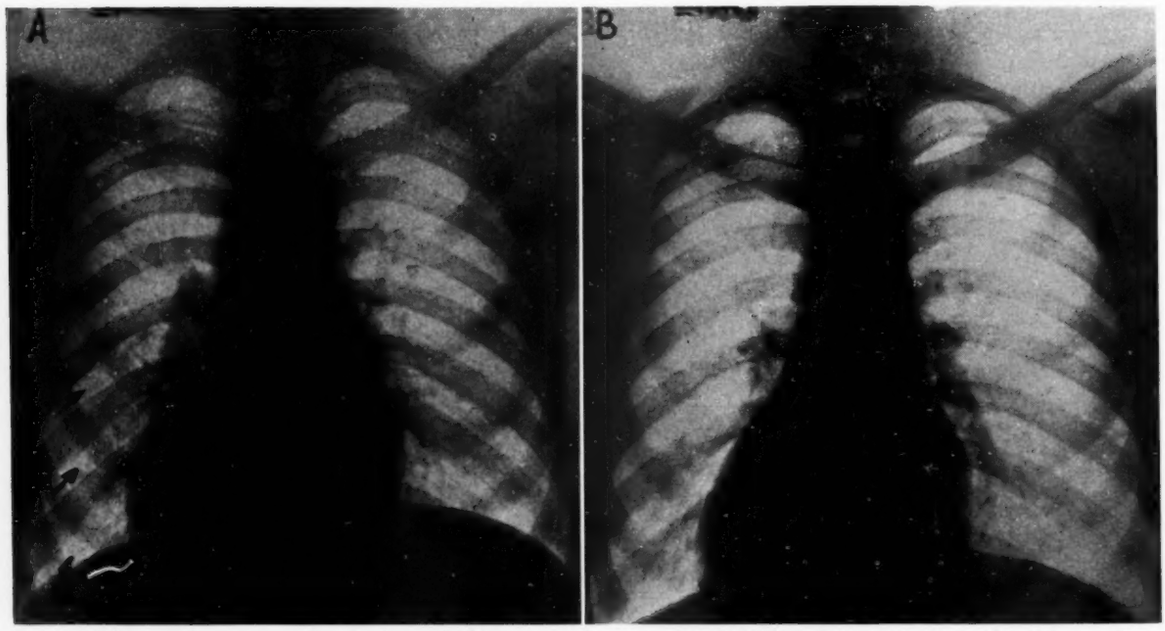


FIG. 2. Rheumatic pneumonia. A, irregularly scattered areas of soft infiltrations throughout both lower lung fields, more marked on the left side. Onset of pneumonic involvement occurred the previous day. B, marked diminution in extent and intensity of the infiltrations the following day illustrating the transient nature of the exudates.

come to postmortem examination. It may occur on either or both sides and usually follows pulmonary or pericardial involvement.[5] Characteristically, the initial severe inspiratory pain and friction rub disappear within several days as effusion accumulates. Routine roentgenograms demonstrate fluid levels in a high percentage of cases. Aspiration is seldom required but shows a clear or cloudy serofibrinous exudate. On rarer occasions it may appear hemorrhagic, possibly due to the presence of pulmonary infarction. Although the fluid is rapidly absorbed, adhesions develop occasionally. These may be pleuropericardial adhesions which give the cardiac silhouette a scalloped appearance or partially obliterate the pleural space.

MITRAL VALVULAR DISEASE

Several pulmonary complications commonly occur following distortion of the mitral valve. On rare instances mitral stenosis may be associated with an interauricular septal defect (Lutembacher's syndrome).

Chronic Congestive Failure. Mitral valvular lesions, especially stenosis, may produce early pulmonary congestion. As a result of chronic congestive heart failure the lungs become firm, dense, dry and red-brown in appearance. There is interstitial edema, increased collagen and thickening of the capillary basement membrane. These changes thicken the alveolar wall and interfere with gaseous exchange. They eventually produce an inelasticity of the lung tissue which seriously interferes with ventilation.

Dyspnea, orthopnea and cyanosis are major symptoms. Hemoptysis occurs in 10 per cent of cases of mitral stenosis due to vascular hypertrophy. Although it may appear at any time during the course of the disease, it usually denotes an advanced degree of stenosis with increasing pulmonary congestion. The blood loss is seldom massive but augurs a dire prognosis. Cough is commonly present, and when productive the sputum may reveal numerous "heart failure" cells. The sputum is mucoid but may be blood-streaked or frankly purulent due to secondary bronchopulmonary infection.

Acute Pulmonary Edema. This may occur in mitral stenosis and other valvular lesions even when regular sinus rhythm exists. It usually follows severe exertion, operation, pregnancy, rapid digitalization or paroxysmal tachycardia. Attacks are precipitated by the added strain on the right heart in the presence of pulmonary congestion. Treatment includes digitalization, morphine and atropine, oxygen, mercurials and antifoaming agents.[6]

Subsequently, surgery may be indicated. Remarkable results are constantly being reported by numerous surgeons. Commissurotomy or finger fracture of the stenosed valve, or anastomosis between the aorta and pulmonary artery or between the right inferior pulmonary vein to the azygos veins will relieve pulmonary hypertension.

Rupture. Rupture of a papillary muscle of chordae tendineae results in an unusually rapid form of pulmonary congestion. This may be caused by trauma, superimposed subacute bacterial endocarditis or coronary thrombosis. It produces an extremely loud murmur which is frequently audible at a distance from the chest.

Pulmonary Infarction. The effects of pulmonary infarction are discussed elsewhere. Suffice it to say that this serious complication may result from the discharge of clots from the right auricle during auricular fibrillation. It is important not to overlook other major causes such as peripheral or pelvic venous thrombosis. Early treatment of the primary heart condition and the use of anticoagulants have greatly reduced morbidity and mortality. Amputation or ligation of the auricular appendages is presently employed with success in cases with recurrent embolization (Madden).

BACTERIAL ENDOCARDITIS

The acute and subacute forms of bacterial infections of the valvular and mural endocardium may be caused by many microorganisms. However, the non-hemolytic streptococcus accounts for 95 per cent of all cases. In order for emboli to reach the lungs, the right heart must obviously be affected. Septal defects, pulmonary or tricuspid stenosis, patent ductus arteriosus, tetralogy of Fallot or other combined congenital lesions may also provide a nidus.

Pulmonary emboli and infarctions, congestion, bronchopneumonia or lung abscesses may be encountered. The infarctions usually are too small to be visualized on the x-ray. Pleural effusions or hemorrhages are not uncommonly found. Emboli in pulmonary arterial branches may also result in arteritis or mycotic aneurysm. Symptoms include cough, chest pain, dypsnea or bloody expectoration. Antibiotics are effective in most cases when properly selected and administered in adequate dosage.

ACUTE NON-SPECIFIC PERICARDITIS

Acute pericarditis is usually regarded as evidence of serious underlying disease such as rheumatic fever, myocardial infarction, uremia, tuberculosis and pneumonia. There is a rarer group of disorders which may also produce acute pericarditis. However, we are primarily concerned with acute non-specific pericarditis. This type occurs in young males as a rule and has an increasing incidence. Frequency of recurrences has been emphasized lately.

Invariably there is involvement of the pleura in viral inflammation of the pericardium. A pleural lesion must be suspected when the clinical (chest pain, dyspnea, fever, rub) and laboratory findings (electrocardiogram and x-ray) of acute non-specific pericarditis are accompanied or followed shortly by the onset of a pleural friction rub which may last for days or weeks. This may progress to pleural effusion of varying degree (usually small in amount) and, finally, progressive pleural thickening. The aspirated fluid is exudative and non-bloody and may be bilateral.[7] Pulmonary involvement is uncommon. Pleural fluid is demonstrable on the roentgenogram. Persistence of fever, following improvement of the pericarditis and invariable recovery further suggest this possibility. Results with aureomycin, chloromycetin® and terramycin® have been equivocal thus far. The disease is self-limited but aspiration of fluid is indicated when its presence embarrasses cardiac or pulmonary function. (Fig. 3.)

CHRONIC CONSTRICTIVE PERICARDITIS

Chronic constrictive pericarditis is a dense fibrous thickening of the pericardium (Fig. 4) which may cause compression of the heart and interfere with normal filling. It may completely envelop the heart or produce a band-like or other localized strictures. It is characterized clinically by the triad of a small quiet heart, elevated venous pressure and ascites.

The cause is often obscure. Although tuberculosis is the most common cause in cases with proven etiology, this disease accounts for only 15 per cent of all cases. Rheumatic fever, pleuropulmonary disease, myocardial infarction and neoplastic involvement make up the bulk of all cases. (Fig. 4.)

The lungs usually do not reveal significant congestion or fibrosis unless tuberculosis is the

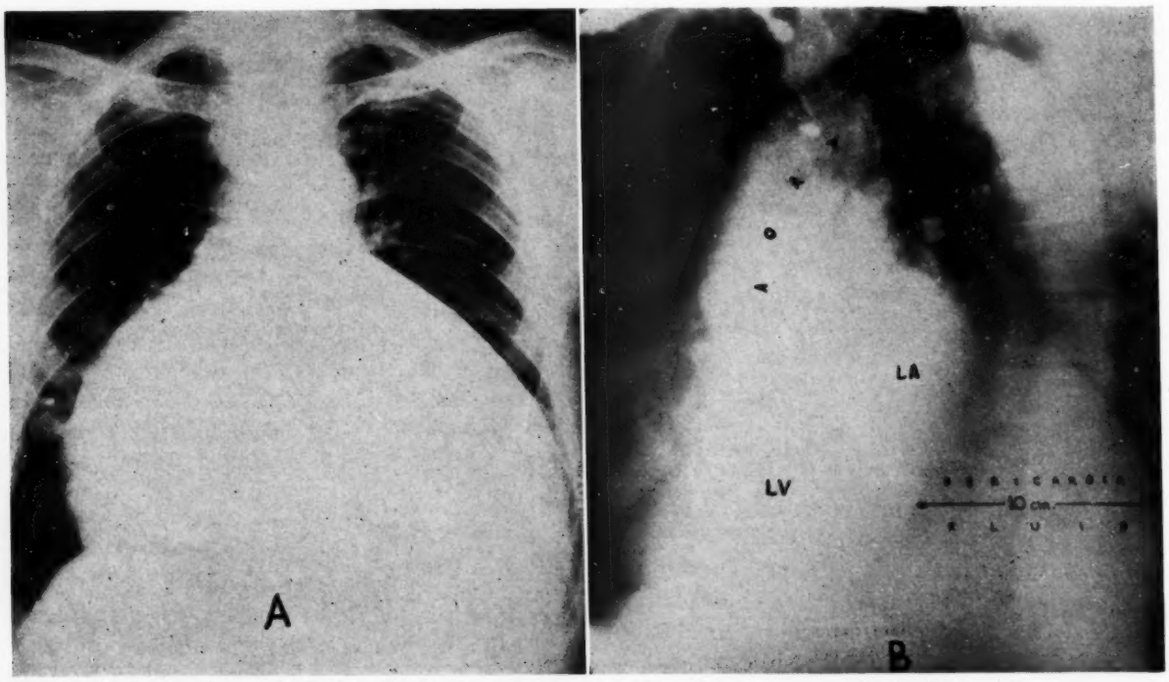


FIG. 3. Marked pericardial effusion. Reduction of pulmonary function by very marked effusion. A, note water-bottle configuration of pericardial effusion. B, in left anterior oblique view of angiocardiogram the pericardial effusion is more sharply defined. Note posterior compression of lung space.

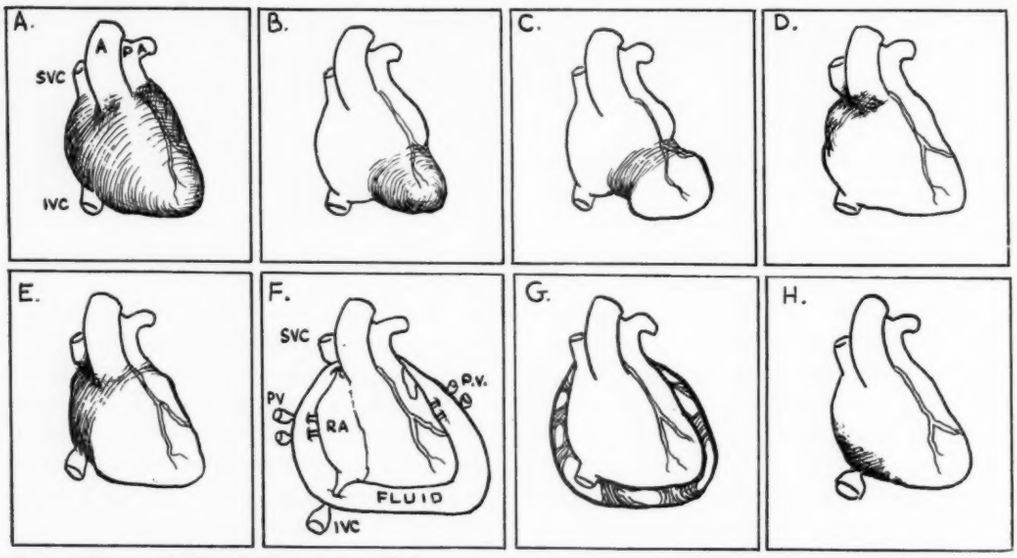
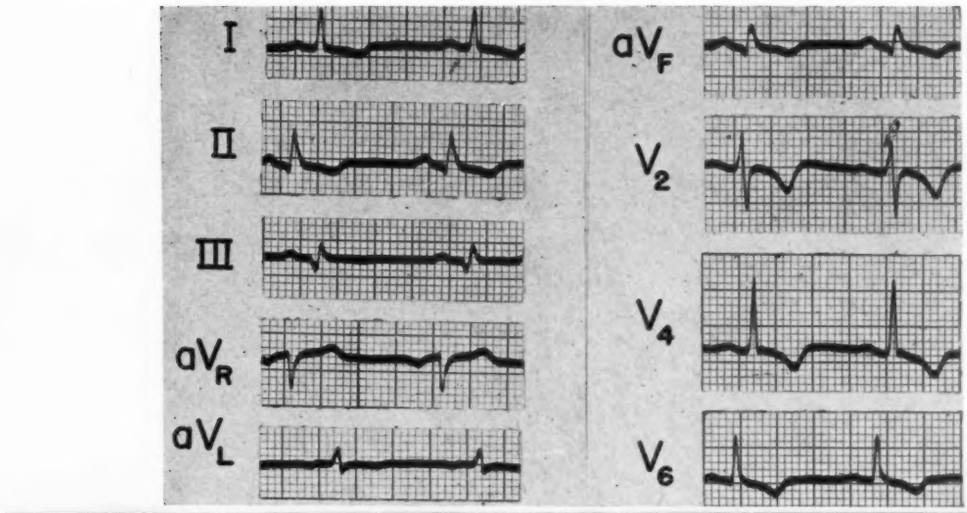
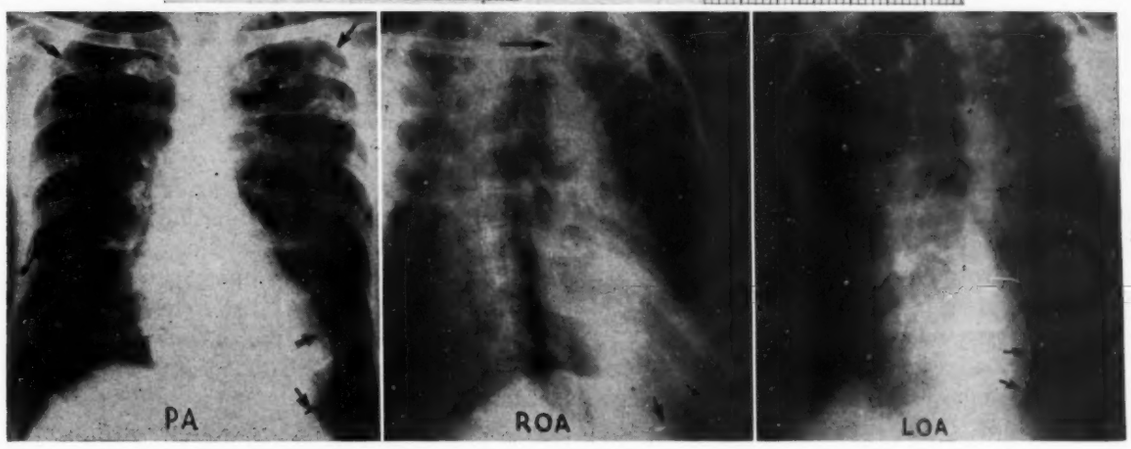


FIG. 4. Types of chronic intrapericardial pressure. A, complete enveloping scar. B, ventricular scar; note compression with bulge above. C, band over ventricles. D, band around superior vena cava, resulting in superior vena caval syndrome. E, band over auricles. F, tamponade (blood or effusion); note compression of auricular appendages and intrapericardial portions of venae cavae and pulmonary veins. G, adhesive pericarditis. H, band around inferior vena cava, resulting in inferior vena caval syndrome. (From REICH, N. E. The Uncommon Heart Diseases. Springfield, Ill., 1954. Charles C Thomas.)



5A



5B

FIG. 5. Chronic constrictive pericarditis. A, electrocardiogram reveals negative T waves and decreased voltage of QRS complexes. B, x-rays reveal chronic tuberculous pericarditis with bilateral apical lung involvement. Arrows point to calcification.

cause. (Fig. 5B.) Yet pleural adhesions or effusions are fairly common. When the constricting pericardial scar is localized mainly over the left auricle, relaxation and filling of this chamber may be seriously interfered with. Constriction around the pulmonary vein orifices may result in marked pulmonary engorgement.[7] Dyspnea may be due to extensive pleural effusions, pulmonary congestion or decreased vital capacity owing to marked elevation of the diaphragm by ascites. The vital capacity was reduced up to 68 per cent of normal in the cases reviewed by Stewart and Heuer.[8] Signs of cardiac fixation and evidences of the right heart failure syndrome comprise the cardiac findings. The electrocardiogram is characteristic. (Fig. 5A.)

Medical treatment is of little avail when signs of cardiac or pulmonary embarrassment appear. Dramatic improvement occurs following decortication of the heart. This was first practiced by Cutler as far back as 1924. Streptomycin, PAS and isonicotinic acid derivatives are of value in the treatment of active tuberculous lesions.

SYPHILIS

It has been estimated that a quarter of a million Americans have cardiovascular syphilis, yet only 2 per cent of these develop aneurysm.[9] The unfavorable prognosis of cardiovascular syphilis is well known. Aortic valvular lesions are generally considered to be more serious than mitral lesions because they are often caused by neglected syphilis and because of

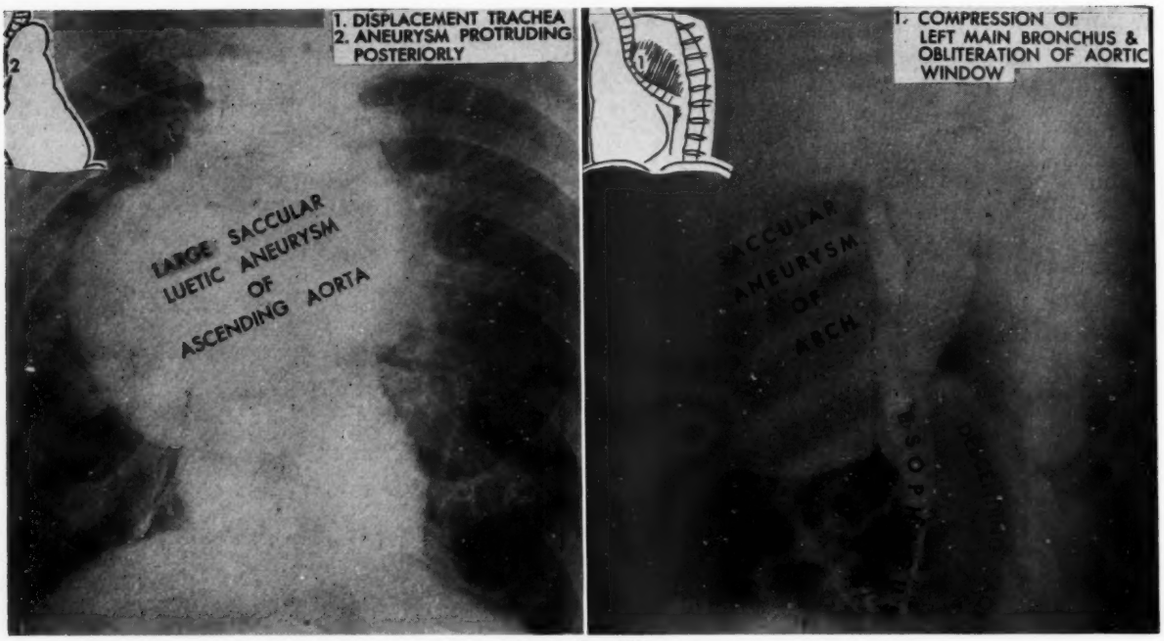

1. DISPLACEMENT TRACHEA
2. ANEURYSM PROTRUDING POSTERIORLY
LARGE SACCULAR LUETIC ANEURYSM OF ASCENDING AORTA
1. COMPRESSION OF LEFT MAIN BRONCHUS & OBLITERATION OF AORTIC WINDOW

FIG. 6. Syphilis.

the poor prognosis. When left ventricular failure ensues, pulmonary edema is rapid and relatively unresponsive to therapy. Syphilitic myocarditis is equally difficult to treat in the stage of congestive failure.

Saccular aneurysms may reach alarming proportions and may produce symptoms and signs of compression of the lungs, bronchi and other structures depending on the direction and extent of their dilation. (Fig. 6.) Aneurysms of the arch are most important because of their greater proximity to respiratory structures. Pulmonary signs of atelectasis, bronchiectasis and secondary infection may result. Tracheal tug may be elicited and left recurrent laryngeal nerve compression may result in hoarseness or aphonia. Phrenic nerve involvement may produce paralysis of the diaphragm, thereby interfering with oxygenation.

The most important of these complications is *atelectasis*. Unless the pathologic condition is sufficiently extensive, tactile fremitus may be non-revealing.[10] Diminished breath sounds and altered resonance on percussion may be noted. Bronchiectasis may ensue from lack of drainage and infection induced by bronchial compression.

Endobronchial tumors and other lesions must be differentiated occasionally. Bronchography may reveal the true cause of localized obstructions or distortions of the bronchial tree. Tomography may exclude endobronchial tumor by delineating cavitation within the aneurysmal mass. This is unreliable when the aneurysm is clotted. Kymography may show typical expansile pulsations when the aneurysm is unclotted. Further differentiation of adenoma, carcinoma and inspissated mucous or granulomatous tissue rarely requires cautious bronchoscopy, biopsy or Papanicolaou staining of sputum for tumor cells. Serology is positive in approximately 85 per cent of cases. Calcification in the wall of the ascending aorta (left anterior oblique view) is characteristically found in approximately half of all cases of luetic aortitis.

Antibiotics now have a definitely established position in the treatment of cardiovascular syphilis. Aneurysms have been wired and electrocoagulated, or surrounded by various cellophanes in order to produce a fibrotic reaction which will shrink or prevent further expansion with rupture.

MYOCARDIAL INFARCTION

This condition has already received the direct attention of surgeons. Not only are a number of surgical procedures available pertaining to revascularization of the heart, but also excision of large myocardial scars and aneurysms is being practiced presently.

A number of pulmonary complications is possible in patients suffering from myocardial

infarction. They are mistakenly referred to as "pneumonia" in most instances. Five conditions must be considered when lung findings appear following this condition.

Pulmonary Edema. This dire pulmonary complication is due to acute left ventricular failure, since the left ventricular musculature is most commonly affected by infarction. It may be the dominant manifestation of an acute myocardial infarct appearing suddenly within hours to days following an occlusion.

Symptoms include thoracic oppression, dyspnea, orthopnea and cough. The attack may be characterized by episodes of paroxysmal nocturnal dyspnea with wheezing respirations and rhonchi. Mild pulmonary congestion is common when the dominant manifestation is pain, shock or congestive heart failure. Basal rales are heard in such cases, especially on the right side. It may become more severe with noisy respirations when copious white or pink foam appears. In advanced cases it may pour out of the oronasal passages and bubbling rales may become audible up to the apices. Digitalis, oxygen, morphine and atrophine, diuretics and antifoaming agents are employed.[6] Anticoagulants are also employed since they affect the ultimate prognosis.

Atelectasis. It is very common to find a localized patch or patches of crepitant rales at the left lung base, coinciding with x-ray demonstration of plate-like areas of atelectasis. However, this is found so frequently early in the attack that it is usually considered normal by Wolff and not necessarily indicative of congestive failure, pulmonary infarction or infection.[11]

An area of dullness and bronchial breathing without temperature elevation usually indicates the presence of atelectasis. Oxygen and expectorants may be of value in such cases. Rebreathing is obviously contraindicated following myocardial infarction.

Pneumonia. Pneumonia is rarely associated with acute myocardial infarction and yet this diagnosis is made with alarming frequency and treated as such. The possibility of other lesions such as localized pulmonary edema, pulmonary infarction, atelectasis or chronic bronchiectasis must be investigated. When there is leukocytosis, hyperpyrexia and mucopurulent sputum, a therapeutic trial with an antibiotic is indicated.

Localized Pulmonary Edema. This complication is not uncommon in acute myocardial infarction and is usually bilateral. The condition is commonly confused with pneumonia or pulmonary infarction. In addition to dullness or flatness and bronchial breathing, a shower of fine inspiratory rales is frequently heard. The clinical course is usually severe with frank hemoptysis, marked pyrexia, and leukocytosis. Signs of congestive failure may ensue in some patients. The x-ray picture is diagnostic.[11]

Pulmonary Infarction. Emboli to the lung may be due to auricular fibrillation, peripheral and pelvic venous thrombosis, bacterial endocarditis and right-sided mural thrombosis owing to myocardial infarction. Emboli may enter any part of the pulmonary arterial system although the right base is commonly affected. The sudden onset of chest pain, cough and bloody expectoration usually heralds this complication. Signs include a patch of crepitant rales, dullness and bronchial breathing. Pleural pain is present in half of the cases but a rub occurs in only 10 per cent of the cases.[12] Effusions are usually minimal and may be clear or sanguineous. On rare occasions large recurrent effusions may dominate the clinical picture. These effusions seldom require aspiration. The icterus index may be slightly elevated on the second or third day due to absorption. The electrocardiogram is diagnostic in a large percentage of the cases, but x-ray investigation is usually disappointing. Immediate anticoagulant therapy is indicated. High venous ligation must be considered when embolization from the peripheral or pelvic veins is suspected. Inferior vena caval ligation produces peripheral edema which may be quite disabling for long periods.

DISSECTING ANEURYSM

There has been a marked improvement in the recognition of dissecting aneurysms during the last decade. (Fig. 7.) This has been occasioned by an awareness of the disease on the part of most clinicians. Efforts at limiting the pathologic condition to a single factor have been generally unsuccessful although medial necrosis is recognized as the most important pathologic factor.[1] Pulmonary symptoms are rare in the absence of rupture although cough and hemoptysis may occur. When not instantly fatal, various clinical syndromes may appear depending on the site and extent of dissection or rupture.

Twenty per cent of all dissections rupture into the left pleural cavity and present the

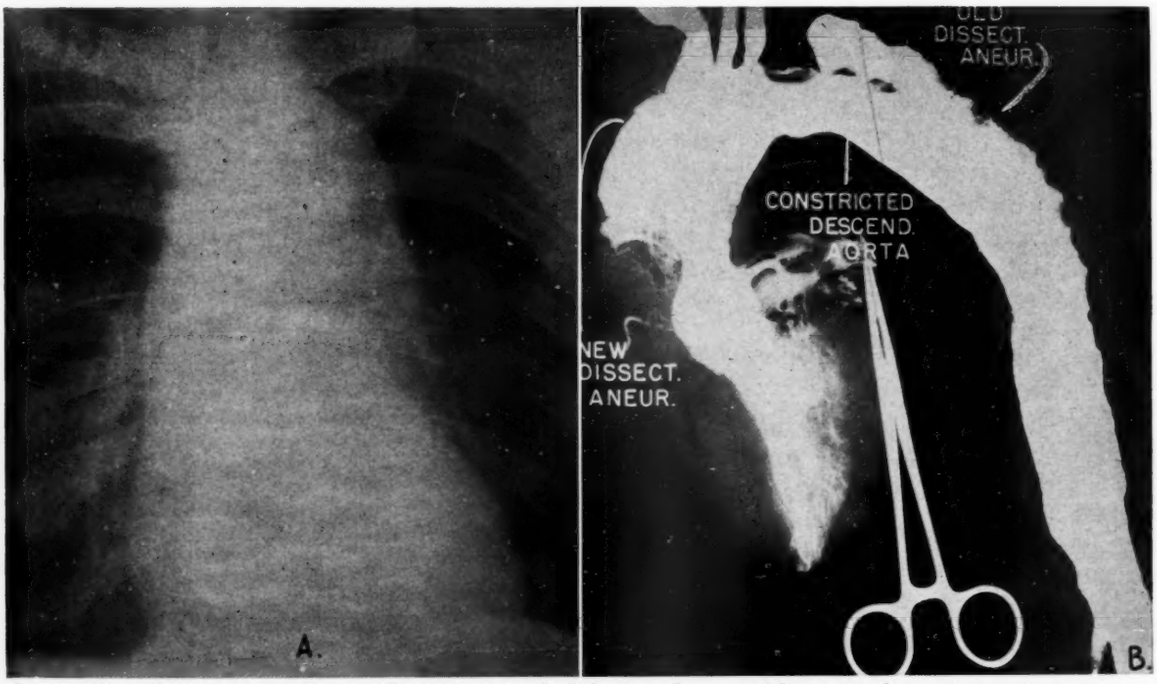


FIG. 7. Dissecting aneurysm. Eventual rupture into the left pleural space with massive hemothorax. A, roentgenogram prior to rupture. B, injected specimen.

characteristic signs of chest fluid.[13] However, fluid in the left pleural cavity must be differentiated from tuberculosis circulatory failure (which seldom affects the left side alone), malignancy of the pleura and Meig's syndrome. The aspiration of pure bloody fluid is highly significant for dissection. Malignancy may reveal characteristic cells in addition, and tuberculosis may show organisms on smear or culture. On rare occasions ruptures into the right pleural and retroperitoneal space, mediastinum and other structures have been described. Massive hemoptysis may indicate rupture directly into the trachea, bronchi or lung.

Blood replacement and pleural aspiration are indicated. Enzymatic agents (tryptar,® or streptokinase and streptodornase) are capable of liquefying blood clots prior to aspiration. Surgical repair of the site of rupture may be attempted by employing gelatin sponge cuffs or by applying polythene cellophane (PT 300). Occasional cases are known to heal spontaneously.

NEOPLASMS

Although primary tumors of the heart are relatively rare, metastatic lesions are not uncommon. Metastatic lesions may arise from any tissue in the body, the most common sources being the trachea, breast, lung and stomach. On rare occasions they may produce the syndrome of chronic constrictive pericarditis. Primary neoplasms occur approximately once in every 2,000 cases that come to autopsy.[14] The frequency of types has been reported in the following order: myxoma, sarcoma, rhabdomyoma, fibroma, lipoma, angioma, cystoma, papilloma, teratoma and epicardial epithelioma. Any heart chamber may be the site of neoplasm, but the right side is more commonly involved. Therefore, pulmonary metastases from primary cardiac malignancies are frequently found.

Diagnosis of a primary lesion should be suspected in cases of heart disease of undetermined etiology when: (1) roentgenogram shows an unexpected or bizarre heart size or shape, (2) there are progressive electrocardiographic changes otherwise unexplained, (3) pericardial aspiration reveals red cells and tumor cells, and (4) frequently changing arrhythmias and murmurs appear. Pedunculated intracardiac tumors may produce intermittent obstruction of valve orifices and simulate valvular lesions. The subsequent appearance of metastatic pulmonary lesions with or without pleural involvement should increase the index of suspicion.

This is especially true when pleural transudates also contain tumor cells or when stained bronchial secretions reveal tumor cells of non-carcinomatous origin. (Fig. 8.)

Treatment may be effective when the tumor is benign and pedunculated. Such tumors have been removed from within the heart (Beck, Bailey). The development of a good mechanical heart will permit more extensive surgery. Radiotherapy and chemotherapy have produced no known cures thus far, although life may be prolonged in some cases of malignant lymphoma. Urethane, nitrogen mustard and certain radioactive isotopes have proven of some benefit in appropriate cases.

TABLE I

DISEASES OF THE LUNG PARENCHYMA*

1. *Infections*
   Acute pneumonitis, chronic bronchitis, bronchiectasis, chronic bronchopulmonary suppuration; various virus and rickettsial diseases
2. *Infectious Granulomas*
   Tuberculosis, sarcoidosis, fungus infections
3. *Parasitic Diseases*
   Chagas' disease and schistosomiasis are excellent examples
4. *Allergies*
   Bronchial asthma and allergic bronchitis (with secondary emphysema)
5. *Chemical and Physical Irritants*
   Dusts, fumes, gases, x-ray and radium fibrosis. (Included are the various pneumoconioses of which silicosis, anthracosis and beryllosis are the most important.)
6. *Malignancies*
   Extensive primary or metastatic malignancies. (Metastatic endolymphatic carcinoma is the most common cause.)
7. *Miscellaneous Diseases*
   Pulmonary amyloidosis (primary systemic and secondary forms), pulmonary fibrosis and emphysema due to various causes, congenital cystic lung disease, massive pulmonary collapse, extensive pleural adhesions, chronic passive congestion (secondary sclerosis)

* Tables I to IV from REICH, N. E. The Uncommon Heart Diseases, Springfield, Ill., 1954. Charles C Thomas.

CHRONIC COR PULMONALE

Chronic cor pulmonale is a term applied to hypertrophy of the right ventricle, with or without congestive heart failure. Despite a varied etiology which includes a number of pulmonary (Table I), cardiac (Table II) and vascular disturbances (Table III), and bony cage deformities (Table IV), increased resistance and pressure in the pulmonary circuit is the basic mechanism.[7] Since we are considering the pulmonary complications of primary heart disease, the other factors will not be considered in any detail. However, it is significant that when congestive failure supervenes, other pulmonary findings become superimposed on the underlying lung disease process (e.g., pulmonary emphysema and other bronchopulmonary diseases).

FIG. 8. Syphilis with malignancy in a sixty-one year old man. Note aneurysmal dilation of thoracic aorta and large bronchogenic carcinoma invading mediastinum with metastases to right upper lung field. Autopsy corroboration.

TABLE II

PRIMARY HEART DISEASES

1. Mitral valve involvement
   a. Mitral stenosis
   b. Lutembacher's syndrome (mitral stenosis with interauricular septal defect)
   c. Subacute bacterial endocarditis
2. Left ventricular failure, due to myocardial infarction, amyloid disease, beriberi, etc., but most frequently due to aortic disease or hypertension. (None of these will show right axis deviation but may have pulmonic hypertension, right ventricular hypertrophy and failure.)
3. Auricular fibrillation (with right auricular thrombus producing pulmonary emboli)
4. Chronic constrictive pericarditis affecting the left auricle
5. Tumor of heart causing mural thrombi and pulmonary embolism
6. Congenital defects (patent ductus, septal defects, aberrant pulmonary veins)

Kyphoscoliosis, funnel chest and other chest deformities are interesting in that they may also cause hypertrophy and dilation of the

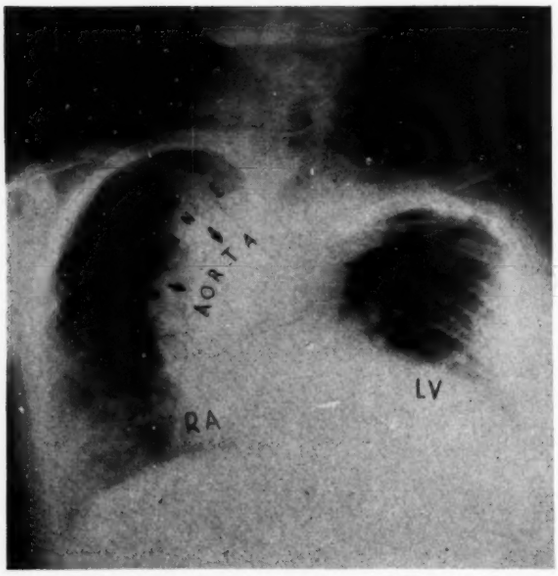


FIG. 9. Kyphoscoliotic heart disease. Marked rachitic spinal deformity in fifty-eight year old woman. Severe exertional dyspnea. Note spinal curvature toward right eventually producing chronic cor pulmonale. Note prominent pulmonary vessels, atelectasis at bases with compensatory emphysema.

right ventricle. It is the consensus that the syndrome occurs in about 75 per cent of cases of severe kyphoscoliosis. (Fig. 9.) These deformities may also produce compression atelectasis or secondary emphysema in addition to bronchopulmonary infections.

The diagnosis of chronic cor pulmonale is based upon the recognition of the underlying causative factor (Tables I to IV) and the discovery of right ventricular enlargement with or without evidences of failure. Right-sided failure is recognizable by the presence of hepatomegaly, dependent edema and ascites, elevated venous pressure and prolonged arm-to-lung circulation time. It is important to remember that dyspnea and cyanosis are usually due to the underlying lung or heart disease, but may be aggravated in the presence of congestive failure.

Roentgenologic studies show: (1) an exaggeration of the hilar markings due to enlargement of the pulmonary artery and its major branches; (2) enlargement of the right ventricular outflow tract in the left anterior oblique view as indicated by the posterior displacement of the interventricular groove, and in the right lateral position by the encroachment of the right ventricle on the retrosternal space; and (3) prominence of the pulmonary segment in the postero-anterior view. (Fig. 10A.) When decompensation intervenes, (1) the right auricle may become enlarged, (2) there is enlargement of the right ventricular inflow tract as well, (3) the transverse diameter of the heart is further increased in size, (4) the lower lung fields reveal congestive changes or fluid. Electrocardiograms show a progressive right ventricular strain pattern. (Fig. 10B.) Pulmonary function tests are employed in the evaluation of the lung status. The vital capacity is markedly diminished. Dyspnea is out of all proportion to the cardiac state and is mainly due to the associated pulmonary disease.

Treatment must be directed at the causative lesion as well as myocardial insufficiency. In many disorders, such as kyphoscoliosis, it is unsatisfactory. In others, such as patent ductus arteriosus, early surgical intervention results in complete relief. When dyspnea and cyanosis occur due to either cardiac or pulmonary fac-

TABLE III

DISEASES OF THE PULMONARY VASCULAR SYSTEM

1. *Pulmonary Arteries*
   - a. Embolism
     - (1) Phlebothrombosis and thrombophlebitis of the peripheral, abdominal and pelvic veins and the venae cavae. (Thromboembolic complications due to myocardial infarction are considered under primary heart disease.)
     - (2) Embolism due to air, fat and foreign bodies (bullets, etc.)
   - b. Endarteritis obliterans (Ayerza's disease)
   - c. Aneurysm (syphilis, congenital, post-stenotic)
   - d. Thrombosis due to blood dyscrasias
   - e. Persistent truncus arteriosus
   - f. Thromboangiitis obliterans, lupus erythematosus disseminatus, polyarteritis nodosa
   - g. Congenital and acquired intravascular bands
   - h. Primary neoplasms of the pulmonary vascular system
   - i. Neoplastic invasion or compression of larger branches
2. *Pulmonary Veins*
   - a. Massive infectious endophlebitis
   - b. Thrombophlebitis migrans
   - c. Neoplastic invasion or compression of large branches
   - d. Thrombosis due to blood dyscrasias
   - e. Aberrant pulmonary veins

TABLE IV

THORACIC BONY CAGE DEFORMITIES

1. Congenital deformities of the chest (funnel or pigeon breast)
2. Kyphoscoliosis due to neuromuscular diseases (e.g., poliomyelitis) and bone diseases (e.g., rickets)
3. Thoracoplasty
4. Ankylosing spondylarthritis

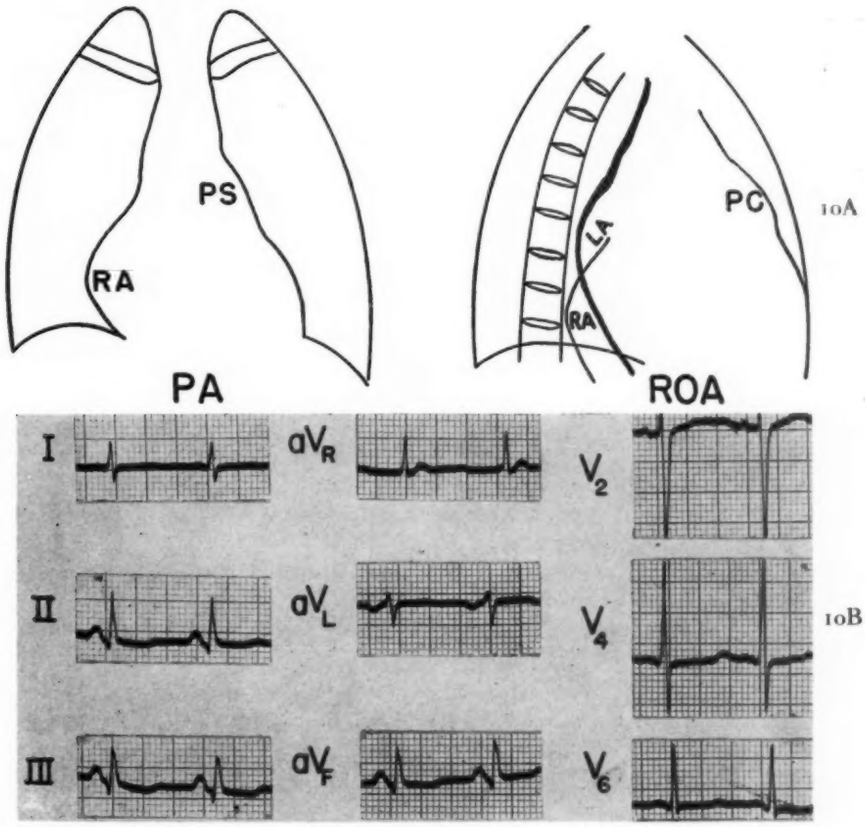


FIG. 10. Chronic cor pulmonale. A, postero-anterior and right oblique anterior views showing chamber enlargements. B, electrocardiogram reveals characteristic changes of right ventricular strain pattern.

tors, oxygen therapy is indicated. Digitalis produces equivocal results in this type of failure but should be given a therapeutic trial. Venesection may prove beneficial in the presence of high plasma and cell volumes. Antibiotics are indicated in the presence of underlying or intercurrent bronchopulmonary infections. Morphine is definitely contraindicated since it depresses respiratory activity. New types of surgical anastomoses are being advocated to relieve pulmonary engorgement in some cases; pulmonary to azygos veins (Swan) and various operations for mitral stenosis. Orthopedic conditions require correction.

SUMMARY

1. The appearance of pulmonary findings during the course of many heart diseases must be evaluated carefully for proper diagnosis, prognosis and therapy.

2. Pulmonary complications may appear following certain congenital cardiac defects, acute and chronic inflammations of the heart and aorta, degenerative lesions of the coronary arteries and aorta, primary neoplasms of the heart and chronic cor pulmonale.

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Arteriovenous Aneurysm of the Lung

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ARTERIOVENOUS aneurysm or fistula of the lung is a congenital shunt between arteries and veins in the lung. This abnormal vascular communication has been designated by a variety of names. Similar terms have been used to describe different pathologic lesions and, conversely, a single pathologic condition has been designated by different names. The lesion to be mentioned in this article appears, on the basis of the pathologic picture, to be a real arteriovenous aneurysm or fistula.[1] Hemangiomas of the lung are neoplasms with a different clinical and pathologic aspect,[53] and the term hemangioma or cavernous hemangioma ought to be reserved merely for these tumors. Lindgren[57] proposes the term aneurysm for congenital lesions and fistula for the rare traumatic shunts. This seems to be more and more generally accepted.

These lesions have attained much interest since 1939 when Smith and Horton[89] made the first clinical diagnosis of an arteriovenous aneurysm in the lung. In 1949 Yater et al.[99] and Quemerch[71] reviewed the literature, and in 1953 the author[64] collected seventy-nine cases from the literature including a new case. At present the number has already surpassed 100.

The true incidence of the anomaly is difficult to evaluate since small aneurysms in the lung may so easily escape diagnosis, both clinically and in routine autopsy studies. It seems to be relatively uncommon, but cannot be extremely rare in view of the fact that more than 100 cases have been recorded during the last fifteen years.

Although the diagnosis is frequently made in the third and fourth decade, arteriovenous aneurysm of the lung has been diagnosed in children and even in the newborn,[14] and is probably congenital in origin. The male:female ratio is about 3:2. In more than half of the cases cutaneous telangiectasis could be demonstrated, and in many telangiectasis was present in near relatives of the patient. Goldman[42] supposes that arteriovenous aneurysm of the lung is a manifestation of hereditary hemorrhagic telangiectasis (Rendu-Osler-Weber's disease, Goldstein's heredofamilial angiomatosis).[43] In many patients this is not obvious, but typical cases of Rendu-Osler-Weber's disease may have pulmonary arteriovenous aneurysm. In such cases the aneurysm may easily be overlooked when the cyanosis is masked by anemia.[19,43] Goldman,[42] Moyer and Ackerman[63] and Glenn et al.[40] have observed the lesion in siblings, and Tobin and Wilder[91] have reported the occurrence of arteriovenous aneurysm in a father and son.

Pathologic Anatomy. In the majority of the cases the shunt is from a pulmonary artery to a pulmonary vein. One or more branches from the artery enter the aneurysmal sac which is drained by a greatly enlarged and often tortuous vein. (Figs. 1 and 2.) The aneurysmal channel is often sinuous and may be partly filled with clots. The wall is often paper-thin, built up by hyalinized fibrous tissue, elastic fibers and remnants of smooth muscle cells. The intima may be unevenly thickened, partly covered by mural thrombi and may show atheromatous lesions which may be calcified. Small compression atelectases and cell infiltration are commonly seen in the surrounding pulmonary tissue.[24] The size may vary from small pinpoint-sized telangiectasis to huge tubular or saccular multilobulated aneurysms occupying the greater part of a lobe. Nearly half of the patients have two or more aneurysms large enough to be diagnosed clinically. Estimated from the records where the localization is described in detail, they may be found in any part of the lungs, but they seem to be most frequently seated in the middle and lower lobes of the lungs. Involvement of the thoracic wall by the aneurysm is rare,[2,7,42] but may greatly complicate the surgical intervention. Brink[15] reports an otherwise typical case in which no aneurysm could be seen, neither on the roentgenograms nor by angiographic examination. He supposes that this may be due to multiple

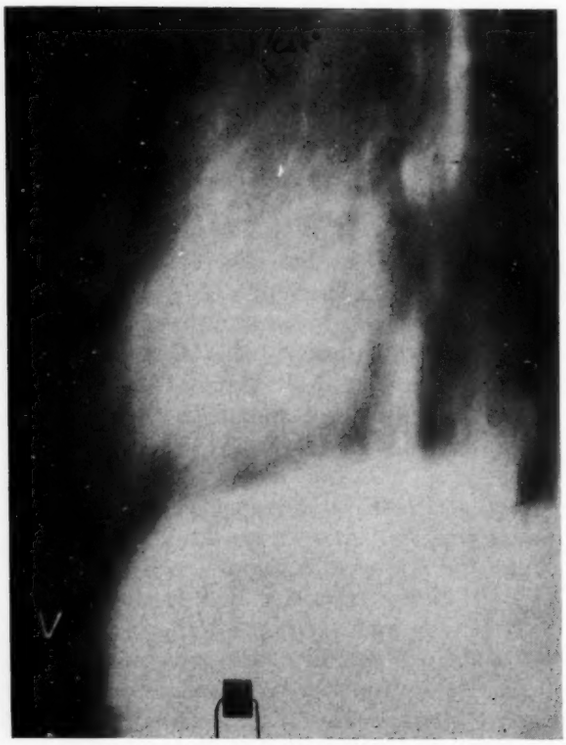

FIG. 1. Oblique tomogram showing the vascular loop of an arteriovenous aneurysm in the L.L.L., hidden behind the heart shadow in the anteroposterior projection.

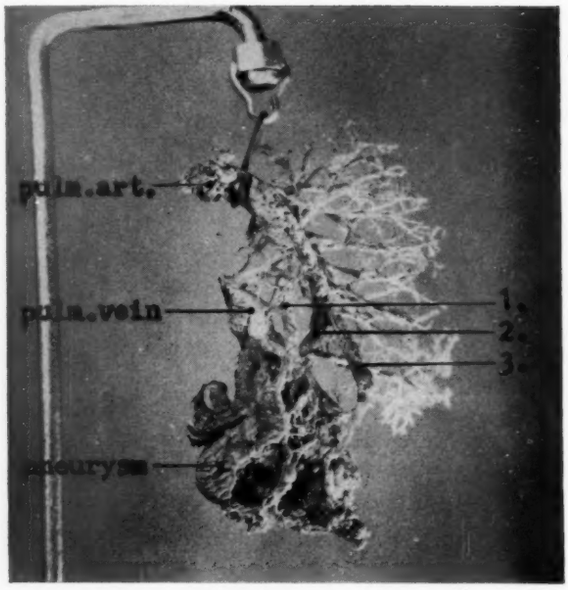

FIG. 2. Same case as Figure 1. Vinylite cast of the vascular tree. The branches not connected with the aneurysm are partly cut away. Three arterial branches enter the aneurysmal sac which is drained by a greatly enlarged vein. (Same projection as Figure 1.)

small arteriovenous aneurysms scattered in the lungs. Grishman et al.[44] emphasize the apparently frequent occurrence of aberrant and accessory pulmonary arteries and veins. This anomaly was also noticed by Sloan and Cooley.[88] In one case reported by Watson[93] the arterial branch to the aneurysm came from the descending part of the thoracic aorta. In other cases without cyanosis the "feeder artery" may be a branch from the bronchial arteries.[60]

Physiology. When the aneurysm is built up by a pulmonary artery and a pulmonary vein, a right-to-left shunt will be established leading to arterial oxygen unsaturation in the systemic circulation. The hypoxemia will give rise to secondary polycythemia with augmentation of the cell volume while the plasma volume remains normal or nearly so. As distinct from the systemic circulation the vascular resistance in the lungs is normally so low that the presence of a shunt will usually not significantly reduce the over-all vascular resistance of the lungs. Moreover, in the presence of a pulmonary arteriovenous aneurysm the capillary resistance in the lungs is higher than normal,[35] probably because of the hypoxemia or caused by multiple thrombi in the lung capillaries as described in the tetralogy of Fallot. In accordance with this, estimations of the cardiac output will usually be within normal limits and right heart failure is rarely seen. If, however, the shunt is so large (in the case of Lequime et al. 89 per cent of the blood passed through the shunt[56]) that the pulmonary vascular resistance is reduced, the cardiac output will be raised and right heart hypertrophy ensues.[7,26,28,35,56] In a case described by Baker and Trounce[7] the cardiac output was estimated to be 12 L. per minute with 80 per cent passing through the shunt. In the presence of systemic hypertension or valvular heart disease hypertrophy may exist independent of the pulmonary shunt.

Symptoms and Signs. Shortness of breath is the chief complaint of most patients. The dyspnea, however, is often less pronounced than what should be allowed for the degree of cyanosis which, besides the clubbing of the fingers and toes, is the outstanding feature in the majority of patients. Nervous symptoms in the form of headache, thick speech, faintness, dizziness, transient numbness and weakness in one side of the body, and convulsions is a com-

mon occurrence in cases with marked cyanosis, probably caused by local anoxemia or small air embolies in the central nervous system.[35,57] Chest pain, usually sharp in nature, radiating and transient, is a major complaint in some patients. Hemoptysis is frequently the symptom that brings the patients to seek medical advice, and may be the terminal event following rupture of the aneurysm into a bronchus.

TABLE 1

Physical Findings	Present	Absent or Not Mentioned
Cyanosis and/or clubbing	91	26
Telangiectasis	62	55
Murmur	61	56

The physical findings in 117 reported cases is summarized in Table 1.

Cyanosis and clubbing of the fingers and toes are the most conspicuous objective signs. The cyanosis may reach extreme degrees depending on the arterial oxygen unsaturation and the hemoglobin value. When a mean of about 5 gm. of hemoglobin per 100 ml. of blood is present in reduced form in the capillaries, cyanosis is visible. In a case reported by Friedlich et al.[35] only 68 per cent of the arterial blood was saturated with oxygen. With a hemoglobin content of 25.3 gm., this means about 8 gm. reduced hemoglobin in the arterial end of the capillary loop.

Telangiectasis in the skin or the visible mucous membranes is found in more than half of the cases and is a valuable clue to the diagnosis. Recurrent epistaxes are frequently reported by these patients.

A murmur, sometimes continuous but more frequently systolic and louder in deep inspiration, is heard in about half of the cases over the site of the aneurysm, and sometimes a thrill can be felt.[70,95]

The heart sounds, which is important, are normal unless unrelated lesions are present. The blood pressure is not elevated, the liver and spleen are not essentially enlarged, and edema is not present.

In some cases cyanosis and clubbing are not present. This may be due to the size of the shunt. Cyanosis will not be visible until about 20 per cent of the blood passes through the shunt, dependent to a certain degree on individual properties of the capillary network in the skin. While cyanosis may be present at birth, it frequently develops in the second and third decade when the aneurysm becomes large enough to shunt a sufficient amount of blood away from the alveolar capillaries. In some cases the cyanosis may be hidden by anemia caused by repeated bleeding from telangiectasis in the nose or in the intestinal tract.[78] In cases of Rendu-Osler-Weber's disease, therefore, roentgen examination of the chest should be performed to detect vascular anomalies in the lungs. When the "feeder artery" comes from the aorta or from a bronchial artery there exists no right-to-left shunt and no cyanosis.[59] In these cases the intravascular pressure must be high and the aneurysm theoretically more apt to rupture than in the ordinary cases with cyanosis.

OBSERVATIONS

Laboratory. In cyanotic cases there is an increase in the erythrocyte count and hemoglobin content of the blood (except in cases with posthemorrhagic anemia). The polycythemia is induced by the hypoxemia in the blood-regulating center.[18,85] Values as high as 11.5 million red blood cells per cu. mm. have been recorded.[41] This will cause a considerable rise in the circulating blood volume, but as the plasma volume remains normal the hematocrit readings will tend to parallel the hemoglobin value. The white cell count is normal. Measurements of the circulation time may show an abnormally short arm-to-tongue time, indicating a right-to-left shunt but not the position of the shunt. The circulation time may, however, be normal even in the presence of a large arteriovenous aneurysm[7] probably because of the great viscosity of the blood. Determinations of the arterial oxygen saturation will give subnormal values, not normalized by oxygen breathing, in cases with a right-to-left shunt. The electrocardiogram is usually normal but may show right axis deviation and high P waves in cases with raised cardiac output.[7,28,54]

Roentgenographic. The most important sign indicating the presence of an arteriovenous aneurysm in the lung is the finding of a shadow in the lung fields on the roentgenograms. The opacity is round or lobulated and connected with the pulmonary hilum by broad, band-shaped vascular shadows. These vessels, even in the case of small aneurysms, are broader

than others situated in the same region, they may have another course and are more sinuous. By the Valsalva test (expiration against closed glottis) the shadow will diminish and conversely, by the Müller test (inspiration against closed glottis) the shadow will augment.[57] By roentgenoscopic examination the shadow may show expansive pulsation. Electrokymography may visualize that the systolic expansions of the mass precedes the normal pulmonary pulse wave.[84] Tomograms may often show the vascular loop more distinctly than an ordinary plate and may also make visible aneurysms hidden behind the shadow of the heart and the liver. The final proof of the vascular nature of the opacity may be given by angiography. The dye will concentrate in the aneurysm and may appear in the left atrium and aorta with abnormal rapidity. Frequently other aneurysms not detected in the plain x-ray film may be visualized. Serious reactions[79] and one death[87] have been reported by this procedure possibly because a too high concentration of the contrast medium (diodrast 70 per cent) reached the coronary vessels via the aneurysm without having been through the mixing effect of the lung capillaries. After all, an angiocardiographic study should be performed in cases in which surgical intervention is being considered, in an effort to establish clearly the extent and number of aneurysms present. Large films covering the whole of both lung fields should be used.

Diagnosis. The majority of these patients have been referred to the medical centers under a provisional diagnosis of congenital heart failure because of the cyanosis and clubbing. Another group of patients are incidentally detected by routine x-ray examination of the chest. In a few hemoptysis and a shadow in the lung fields raise the suspicion of tuberculosis or tumor of the lung. The cyanosis and polycythemia may also lead to an erroneous diagnosis of polycythemia vera.

A complete heart examination will in most cases exclude the possibility of congenital heart failure, a condition which may be present in addition to an arteriovenous aneurysm of the lung.[32,92,95] Other causes of polycythemia must be ruled out. In polycythemia vera chest roentgenograms may show round pulmonary shadows. These are, however, not vascular in nature and disappear after a short time. The white cell count is high with a shift to the left. The blood pressure is usually elevated and the patient looks more red than blue. Pulmonary diseases preventing adequate oxygenation, such as fibrosis and emphysema, will rarely cause cyanosis so pronounced as a right-to-left shunt in the heart or in the lungs. Radiographic examination will be decisive in these cases and moreover, by the shadow of the aneurysm, give a direct clue to the diagnosis. Pulmonary metastases, tumors, cysts, tuberculomas and bronchiectatic sacs filled with secretions may give an appearance which resembles an arteriovenous aneurysm. The important sign to recognize is the relation of the mass to the adjacent vessels which may be demonstrated by tomography and angiography.

The diagnosis is based on the history of the patient and that of the family, physical examination (especially the presence of cyanosis, clubbing, visible telangiectasis and a systolic murmur over the lungs), laboratory and x-ray examination, and ultimately the diagnosis may be confirmed by angiography.

Course. The disease may remain stationary for years if untreated, but frequently there is a definite tendency towards progression, probably caused by a slow enlargement of the shunt or the establishment of new shunts. In the case of Makler and Zion[60] the clinical picture was unchanged after four years, but the hemoglobin value had increased from 19.5 gm. in 1946 to 22.3 gm. in 1950 when the patient was operated upon with a good immediate result.

Of fifty patients who were not operated upon twenty are known to be dead. In seven cases the cause of death was rupture of the aneurysmal sac into a bronchus or into the pleural cavity.[14,32,45,49,77,78,95] Five patients have died from abscess of the brain,[46,55,64,73,98] and Naffziger and Stern[65] have reported two additional cases of arteriovenous aneurysm of the lung complicated by brain abscess. Lindén[55] supposes that these cases are subject to abscesses of the brain caused by paradoxic emboli in the same manner as patients with congenital heart failure. The patient reported by Alexander[3] died from coronary disease. Theoretically these patients may be more vulnerable than normal to coronary stenosis because of the hypoxemia. In one patient the death was caused by angiography.[87] In two cases the cause of death is not mentioned,[25,56] and four patients have died by causes probably not related to the aneurysm.[31,76,81,88] Of the re-

mainder some may have died since the report and, probably, some have been operated upon.

Sixty-seven patients underwent surgical therapy with a primary mortality of 7.5 per cent (five cases).[7,8,21,88,94] One of the patients with bilateral lesions died twenty hours after the second lobectomy.[88] One patient died two and a half years after successful lobectomy.[81]

In five cases[28,35,44,69,93] ligature of the "feeder artery" was performed with improvement in one and a good result in three cases. In one of these patients the arterial branch came from the aorta. One patient had no symptoms before surgery. Another case,[88] not typical in that there appeared to be an almost continuous channel between the pulmonary artery and the left atrium, was cured by ligature.

Removal of the aneurysm was undertaken in sixty-one cases, most frequently by lobectomy. In six cases[16,37,38,40,50,70] the aneurysms were removed by segmental resection, in four cases[12,35,38,60] by lobectomy and excision, and in seven cases[1,41,48,51,63,67,98] pneumonectomy was performed.

Most often the immediate result is excellent, with disappearance of cyanosis in a few hours and a normal return of the blood values in a few weeks. In some cases a certain degree of arterial unsaturation remains which may be caused by additional undiagnosed aneurysms. In cases in which two or more aneurysms are to be removed in a two-stage operation the remaining aneurysm tends to enlarge in the interval between surgery with only temporary amelioration of the symptoms after the first operation.[1,6] Late results are not available.

The indication for surgical therapy is clear in cases with increasing cyanosis, hemoptysis or alarming nervous symptoms. Patients with minimal symptoms run the risk of rupture and cerebral embolism, and intervention in these cases will depend on localization, the number of aneurysms and the age of the patient.

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Pulmonary Embolism Following Mitral Commissurotomy

WITH SPECIAL REFERENCE TO A SUBVALVULAR TYPE

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IN our experience with a large series of cases of mitral commissurotomy we infrequently encountered a massive hemorrhagic clot lodged either in the heart alone or in the pulmonary artery in close proximity to the pulmonary semi-lunar valves. We have come to call these pathologic findings subvalvular and supravalvular pulmonary embolism, depending upon the location of the clot. In a few instances there was simultaneous involvement of the heart and pulmonary artery.

Therefore, with sudden interference of the pulmonary arterial circulation the condition commonly referred to as pulmonary embolism is thought of; however, one should also keep in mind that the obstruction to blood flow may not be in the pulmonary artery but in the outflow tract of the right heart.

The source of ninety-seven fatal pulmonary emboli are given by Fowler and Bolinger[1] as follows: thirty-eight cases originated from the right heart, twenty-six cases from the abdominal pelvis, twenty cases from the extremities, and in thirteen cases the site of origin was undetermined. From our experience with cases following mitral commissurotomy, the site of origin is most likely to be in the right auricular appendage.

The incidence of emboli as shown by Levine and White[2] is: 8 to 12 per cent of routine autopsies, 5 to 10 per cent of postoperative deaths, 31 per cent of autopsied cases of mitral stenosis, and 48 per cent of autopsied cases of congestive failure.

The incidence of pulmonary emboli in surgery as reported by Lam and Hooker[3] are 1 in every 100 prostatectomies or gastric operations, 1 in 500 cholecystectomies, 1 in 600 hysterectomies, and 1 in 1,300 herniorrhaphies and appendectomies.

In over 1,000 cases of mitral commmissurotomy, eighteen patients were diagnosed as having had pulmonary embolism during their hospital stay. Of these cases two occurred preoperatively and sixteen occurred at the time of operation or postoperatively.

Of these eighteen cases, thirteen patients or 72 per cent died. Two patients died within one hour and three died within twenty-four hours. In eight of the fatal cases the patients survived longer than twenty-four hours. Of the thirteen patients who died, autopsy was performed in each case. Of the thirteen cases, it is interesting that five were subvalvular in type, five were supravalvular and three cases were a combination. In the supravalvular type the Trendelenburg operation or its modification by Meyer and Nystrone[4] has been used by others with success in a certain number of cases. In the subvalvular type this procedure would definitely prove unsuccessful, as the outflow tract of the right ventricle, where the clot is found, is not explored. In Cases II and III, as shown in Figures 1 to 4, the clot is clearly discernible in the right atrium traversing and entering through the tricuspid valve into the right ventricle and producing an acute bivalvular obstruction, tricuspid and pulmonary.

CASE REPORTS

CASE 1. E. C., a sixty year old white woman with a diagnosis of mitral stenosis and auricular fibrillation, was operated upon on December 22, 1952.

At surgery a tight mitral stenosis with calcium deposits over the anterior commissure was found. Incisional commissurotomy of the posterior commissure gave a good 1½ fingers

opening. The patient took some time to react from anesthesia but withstood the operative procedure well and made an uneventful recovery. Sutures were removed on January 3, 1953, and she was told that she could go home in a few days.

By 5:00 P.M. on January 3rd she was very dyspneic with elevation of rectal temperature to 99°F., previously subnormal. Thoracentesis of the left side yielded 95 cc. of straw-colored fluid. Smears and cultures of this fluid were returned negative.

The next day she complained of pain and a sense of constriction around her chest. This, coupled with expectoration of blood-streaked sputum, led us to make a diagnosis of pulmonary infarction. Anticoagulants and antibiotic therapy were promptly instituted. The patient felt better on January 5th, but the next day she again started getting dyspneic. Thoracentesis on the left side yielded 228 cc. of fluid which relieved her. X-rays taken on January 4th revealed slight increase in bronchovascular markings in both lung fields (pulmonary congestion).

However, by 1:15 A.M. of January 7th she had a great deal of respiratory distress with bilateral rales over both bases. Her rectal temperature rose to 100°F. Despite oxygen, anticoagulants, mercurials and antibiotic therapy she deteriorated. The total white blood count was 36,000/cu. mm., with 85 per cent polymorphonuclears.

X-rays exaggerated bronchovascular markings in left upper lobe area with elevation of left leaflet of diaphragm.

Heart sounds were poor. There was a fall in hemoglobin counteracted by transfusion of 500 cc. of whole blood slowly.

By 3:50 P.M. the patient had a great deal of respiratory distress when tracheotomy was performed. This was soon followed by disappearance of the apical beat. The chest was immediately opened, with the patient in bed, and massage done. Despite all resuscitative measures the patient died at 5:05 P.M.

At autopsy a bilateral pulmonary infarction with a thin adherent antemortem clot in both right and left auricular appendages was found.

Comment. There was ample time for operative intervention, but the improvement that occurred after conservative treatment was first instituted gave hope that the anticoagulants would prevent further emboli.

CASE II. M. B., a forty-seven year old white woman with a diagnosis of mitral stenosis with atrial fibrillation, was operated upon on January 30, 1953. At surgery the mitral valve could barely admit the index fingertip. The anterolateral commissure was cut, over-all opening 1½ fingers. Blood pressure fell to dangerously low limits before opening of valve (below 60/40). The blood pressure was restored with levophed following commissurotomy. The patient did not react from anesthesia until she was returned to her room.

The postoperative course was stormy, postoperative shock and hyperthermia having developed, the shock not responding to transfusion of blood and vasopressors. Next morning the patient was anuric and not responsive, with a temperature of 105°F. rectally. Tracheotomy was performed to facilitate aspiration of secretions. The fall in temperature was dramatic after the tracheotomy.

On February 1st the blood pressure stabilized to 100/68. The patient's rectal temperature was 100°F. Urinary output was low. The ventricular rate was well controlled. Heart sounds were of good quality.

On February 3rd at 10:00 A.M. she had cold, clammy extremities with a blood pressure of 112/68 mm. Hg. Blood urea nitrogen rose from 44.5 to 70.1 mg. per cent. Urinary output was 100 cc. per catheter. With supportive measures she was well until 7:00 P.M. when she complained of sharp epigastric and left hypochrondriac pain. She also had marked respiratory distress and her rectal temperature rose to 100.2°F. The total white blood count was 29,500/cu. mm., with 93 per cent polymorphonuclears. The question arose whether we were dealing with a case of mesenteric thrombosis or pulmonary embolism due to a clot migrating from the right auricular appendage or even a pericardial effusion owing to the floppy nature of the heart sounds.

At 10:00 P.M. the chest tube was removed and a thoracentesis of the same side was done. Portable film of the chest showed nothing remarkable in the lung fields although the cardiac shadow was enlarged to the right. Pericardial tap was done with much success. The respirations were now 48/min. and very labored. The blood pressure fell to 90/70 mm. Hg.

By 1:30 A.M. of February 4th (five days postoperatively) the patient started to gasp. There

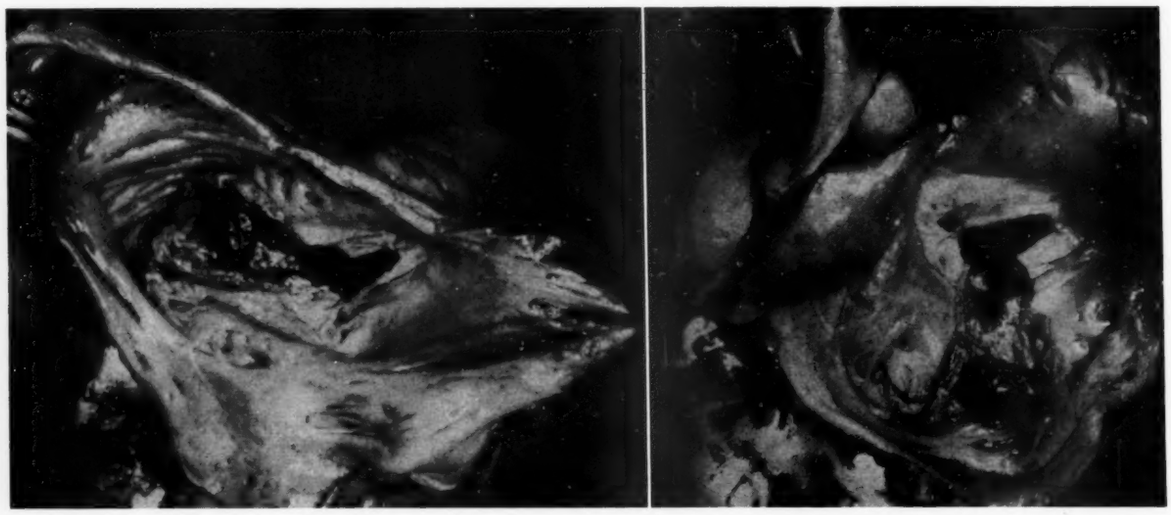

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FIG. 1. From patient M. B. (Case II), showing interior of right atrium with a large antemortem clot originating in the right auricular appendage, traversing the right atrium to enter the tricuspid valve. Within its fold are a few recent clots. As the tail end enters the tricuspid valve, it produces an obstruction to the outlet of the right atrium.

FIG. 2. From same patient, M. B., showing interior of the right ventricle. The onward passage of the clot through the tricuspid valve (left hand, bottom) is shown. The tail end of this widens out in the interior of the right ventricle and finally occupies a position just below the pulmonary valve. Part of it is seen entering the valve orifice.

were very few secretions in the trachea. The chest was promptly opened and the heart beat started by one of us, and a pulmonary artery embolectomy attempted (W. L. J.).

A purse-string suture of No. 5-0 arterial silk was placed around the main pulmonary artery and a catheter inserted through a stab incision, keeping within limits of the purse-string suture. Meanwhile the anesthetist was ventilating the lungs with 100 per cent O_2 through an endotracheal tube inserted through the tracheotomy opening.

Suction of both branches of the right and left pulmonary artery was performed to remove any clots. As it was believed that the blood volume was depleted by suction, a rapid transfusion of 2 pints of blood was given into the cutdown.

Despite all resuscitative measures the patient did not respond and was pronounced dead at 2:35 A.M., February 4th.

At autopsy the right ventricle and right atrium were enormously enlarged. There was a big antemortem clot hanging from the right auricular appendage. The tail end of this clot traversed the tricuspid valve into the right ventricle and through the pulmonary valve into both lung fields. (Figs. 1 and 2.)

Comment. This case illustrates the futility of suction extraction of emboli and of a Trendelenburg procedure which, although clearing the pulmonary artery, does not deal with the main source of trouble (clot traversing tricuspid valve producing relative to complete tricuspid obstruction and thence to pulmonary valve producing a subvalvular obstruction).

CASE III. C. S., a fifty-four year old white woman with a diagnosis of mitral stenosis, mitral insufficiency (minimal) and atrial fibrillation, with previous emboli to the brain, was operated upon on March 25, 1954. At the time of surgery the left atrium was filled with a clot occluding the entrance of the left superior pulmonary vein. The mitral valve was calcific. Digital commissurotomy failed. Both commissures were cut. Hypotension with its sequelae ensued. The over-all opening was estimated at 1½ to 1¾ fingers with 3 to 4 cc. of regurgitation. Some time was spent in ventilating the patient's lungs with O_2 after surgery in the operating room.

On return her blood pressure was 150/90 mm. Hg. She had atrial fibrillation. Heart sounds were normal except for a grade 1 systolic murmur over apex. The rest of the day was spent in combating falls in blood pressure and rises in body temperature to 103.8°F. Hematocrit at 10:30 P.M. was 55 per cent. As chest drainage was 400 cc., a transfusion of 500 cc. of whole

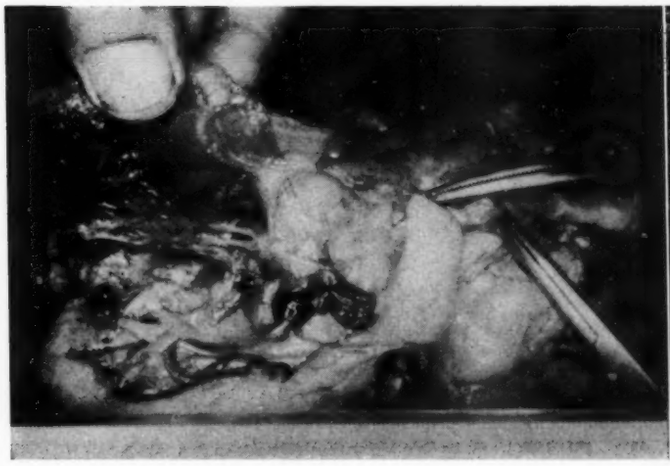

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FIG. 3. From patient C. S. (Case III), showing the interior of right ventricle with the pulmonary artery wide open. The semilunar valves are obscured partially by an embolus. Traced downward the clot can be seen emerging from the tricuspid valve.

FIG. 4. Shows the interior of the right atrium and the tricuspid valve (as seen from the right atrium). The thumb is shown indicating the origin of the embolus as a thrombus in the right auricular appendage. One can visualize how the passage of this huge clot through the tricuspid valve could cause obstruction to the outflow of blood to right ventricle.

blood was given. The patient was cyanotic; lips and fingernails were blue. Plasma, 500 cc., was given when her fingernails turned pink.

On March 26th at 9:00 A.M. she complained of stabbing pain in the chest, which came and went. She was moaning constantly. Anticoagulant therapy was started with heparin, 100 mg. intravenously as initial dose, and coagulation time done with Lee-White method. The dose of heparin was reduced to 75 mg. to keep coagulation time around 20 to 30 minutes. The hemoglobin was 15 gm.; white blood count 21,800/cu. mm.

By March 27th the blood urea nitrogen rose to 70 per cent. Her progress could be summed up as follows: Cyanotic by the hour and O_2 of no avail; blood pressure not responding to vasopressors (levophed and vasoxyl®); temperature rising despite previous fall following ice packing. Respirations rose to 40/min. Tracheotomy was performed with aspiration of a large mucous deposit and some relief. However, she then started getting cyanotic. At 1:30 P.M. the patient had convulsions lasting two minutes, and gasped. Just as she was gasping, the chest was opened by one of us while O_2 under positive pressure was given through a face mask of pneophore and alternate plugging of the tracheotomy opening. Following massage for forty-five minutes and administration of atropine, $\frac{1}{150}$ gr., into the left ventricle, heart action was resumed. The pupils started getting smaller. The heart was replaced into the pericardial sac and the chest closed with a catheter connected to underwater seal drainage. The blood pressure was 120 mm. systolic.

In about one hour she had another bout of arrest from which she never rallied. She was pronounced dead at 3:25 P.M. after attempts at resuscitation.

At autopsy a massive embolus was seen blocking the pulmonary valve. This had its origin in the right auricular appendage and passed through the tricuspid valve into the right ventricle.

Comment. Cardiac arrest developed and the patient was successfully restored. Another cardiac arrest then developed. Cardiac massage was carried out again but the heart did not respond.

Autopsy in this case revealed both subvalvular and supravalvular type of obstruction. (Figs. 3 and 4.) A Trendelenburg operation would have been of no avail in this case. Cardiac massage is of no use in the face of acute tricuspid and pulmonary valve obstruction.

CASE IV. H. A., a forty-six year old white woman with a diagnosis of mitral stenosis and

atrial fibrillation, was operated upon on April 27, 1953. The mitral valve would not admit the tip of the little finger. Following mitral commissurotomy, the valve would admit 2 fingers with production of 5 cc. of regurgitation per heart beat.

The postoperative course was characterized by hypotension, 90/60–30 mm. Hg. There was a low urinary output per catheter and a chest drainage of 1,200 cc. on the next morning.

On April 28th the patient throughout the day had cold clammy extremities, cyanosis and marked hypotension not responding to vasopressors like vasoxyl or levophed. At 5:00 P.M. the blood pressure fell to zero. Whole blood, 500 cc., was given intravenously. She was catherized and 35 cc. of urine obtained. Blood urea nitrogen rose to 38 mg. per cent. Co_2 combining power was 37 vol. per cent. The hemoglobin was 87 per cent; white blood count 46,400 cu. mm.

In view of the hypotension not responding to vasopressors, a cyanosis not responding to O_2 therapy, and in view of her past history of pulmonary infarction, we wondered if we were dealing with a case of pulmonary embolism (only twenty-four hours after surgery).

An arterial transfusion was started in the left brachial artery at 6:30 P.M.; 500 cc. of whole blood were pumped in retrograde fashion in forty-five minutes. The blood pressure rose to 90/60 mm. Hg and the clinical condition improved.

On April 29th the blood pressure maintained around 96/68. The temperature was 100°F. The hemoglobin was 87 per cent; white blood count 27,050/cu. mm. Blood urea nitrogen rose to 54.2 mg. per cent. At 8:45 A.M. the blood pressure fell to 88/68 mm. Hg. The patient complained of some soreness in the chest. By 11:30 A.M. the apical rate rose to 104/min. Morphine sulfate, $\frac{1}{8}$ gr. intravenously, was given for chest pain. At 12:30 P.M. she had lunch consisting of chicken, noodles, ice cream and tea, and said that her appetite was better this day than before. At 1:00 P.M. her blood pressure fell to 86/70 mm. Hg. Occasional twitchings in both hands were noted. She moved her legs a great deal, as a result of which the intravenous cannula slipped. This was restarted. Marked cyanosis was noted over her lips which could not be controlled with nasal O_2. By 1:55 P.M. she started having a convulsion with stiffening of her extremities and marked increase in cyanosis. The chest was opened by one of us at 1:58 P.M. and her heart found at standstill.

Atropine, $\frac{1}{150}$ gr., was given into the cut-down. O_2 was administered through an endotracheal tube. Following cardiac massage and injection of 10 cc. of 10 per cent calcium chloride into the left ventricle, the heart started to beat.

The pulmonary artery was found to be enormously dilated with no pulsations, and the aorta was small and empty.

The pulmonary artery was pinched up with a curved Potts clamp, and a longitudinal incision in the main pulmonary artery about 2 cm. long was made. A large clot was removed from the main pulmonary artery. This clot lodged itself as a saddle-shaped embolus blocking the outflow tract of the right ventricle on the one hand and the right and left branches on the other.

Following the removal of the clot, the incision in the pulmonary artery was closed with a running mattress suture of No. 0000 deknatal. There was approximately 500 cc. loss of blood, and despite all attempts at resuscitation the heart could not maintain its beat and the patient was pronounced dead at 2:45 P.M.

Comment. This case illustrates that the first symptom of pulmonary embolism may be a convulsion. At this time the physicians may wrongly suspect a cerebral embolus.

Earlier surgical intervention may have resulted in success in this case. However, the precarious general condition of many of these patients after surgery together with the lack of a sure means of diagnosis tends to make the surgeon watch the embolus progress to a fatal outcome. Until such time that pulmonary embolism can be diagnosed with certainty and distinguished from other postoperative complications, deliberate operation for removal of an embolus must wait until the patient is in extremis. Crafoord believes that the sign for operative intervention is neck vein distention. We are in agreement with this. It is interesting that this heart responded to massage before embolectomy.

CASE V. R. J., a twenty-seven year old white man with a diagnosis of mitral stenosis, aortic insufficiency and normal sinus rhythm, was operated upon on August 17, 1953. At the time of surgery the mitral valve would barely admit the tip of the index finger. The

valve was opened to 1½ fingers with digital pressure alone. The sternum was transected, opening both hemithoraces. A pericardial pouch was sewn to the ascending aorta. The aorta was opened within the confines of the pouch, and the operator's index finger inserted to palpate the aortic valve. The valve was cartilaginous in consistency. The leaflets were not fused and there was considerable opening and closing. Unfortunately, the closing was not complete. The aortic regurgitation was corrected with a nylon prosthesis. At the end of the procedure the diastolic thrill diminished and diastolic pressure rose to 60 to 80 mm.

The aorta was closed without incidence and the patient did quite well for several hours in spite of persistent drainage. However, by the morning of the following day the blood pressure dropped to 60 mm. systolic and he became cyanotic with respiration ranging from 48 to 64 and labored.

We were unable to account for the deterioration in his condition as blood replacement was adequate. Finally, at 10:00 P.M. he had a bout of cardiac arrest and the chest was promptly opened. Cardiac massage re-established the heart beat but it could not be made to continue independently. The patient was pronounced dead at 10:35 P.M.

At autopsy the right ventricle was hypertrophied and dilated markedly. Attached to the right auricular appendage was a clot which extended down into the triscupid valve. This was firmly attached to the tricuspid and papillary muscles beneath, forming web-like strands of fibrin. It also extended down into the apex of the right ventricle. The tail end of the clot extended to the pulmonary artery in the region of the pulmonic valve. It measured 2.5 cm. in its greatest diameter. On opening the pulmonary artery, no clot was found in the bifurcation. However, dissection of the smaller tributaries involving both lungs revealed fragments of adherent antemortem clots.

Comments. This severe degree of pulmonary obstruction apparently originated from the right auricular appendage. Undoubtedly the atrial fibrillation which had been present for a long time permitted thrombus formation in the right auricular appendage. Transient changes in rhythm causing convulsive contraction of the auricular appendage and expulsion of clots into the blood stream may have precipitated the fatal episode.

Even if a Trendelenburg operation had been performed, the main source of trouble would still have been left untouched (the clot traversing the right auricular appendage, the tricuspid to the pulmonic valve, producing a ball valve subvalvular obstruction). This shows the need for a modification of the Trendelenberg procedures.

REMARKS

In our experience the classical picture of pulmonary embolism of the type under consideration (subvalvular) presents the following aspects: (1) Intermittent recurrent cyanosis not responding to oxygen therapy; we believe this is due to a ball valve effect of the clot, intermittently extending from the right ventricle (where it does not produce obstruction) to the pulmonary valve (where it produces acute obstruction); (2) hypotension not responding to vasopressors; (3) tachycardia out of proportion to any evidence of cardiac failure, pneumonia or other febrile episode; (4) a high white blood count above 20,000 points, with over 80 per cent neutrophils.

A rational approach to the problem is the performance of an immediate thoracotomy and cardiotomy into the right ventricle with simultaneous aeration of the lungs either by an anesthetist or by mouth-to-mouth breathing.

Previous to the time that our attention became focused on the subvalvular type it was believed that an embolus of sufficient size to block the pulmonary artery could be palpated and removed by extraction forceps or suction, as was described in the classic technic of Trendelenburg. However, if the embolus is blocking the pulmonary valve, it would certainly do no good to explore the pulmonary artery.

At the time of operation one may be able to differentiate between the supra- and subvalvular type. In the subvalvular, unlike the supravalvular, the pulmonary artery is flaccid and empty; the right ventricle and right atrium are full with marked distention, the clot acting as an acute obstruction. This condition is even more serious and more difficult to treat than the supravalvular type.

The following technic for extraction of a clot from the outflow tract of the right ventricle has

been formulated after the experience with the cases described herein:

Traction sutures of the type described by Beck[4] for the purpose of controlling cardiac bleeding are quickly placed in the outflow tract of the right ventricle. A stab incision slightly less than the diameter of the operator's finger is then made, and the finger is quickly inserted. The right ventricle, pulmonary valve and tricuspid valve may then be easily palpated. A large clot can be removed by inserting a curved Kelly clamp with the convex side next to the finger, then removing clot, clamp and finger together. The traction sutures are not crossed until the clot is removed. This procedure[5] is similar to that previously described in removing clots from the left atrium. Cardiac massage is then immediately started. During this procedure simultaneous positive pressure administration of 100 per cent oxygen is mandatory.

CONCLUSIONS

1. The site of origin of pulmonary embolism occurring at the time of mitral commissurotomy or after is most likely from the right auricular appendage.

2. A subvalvular type of pulmonary embolism is described.

3. The routine Trendelenburg procedure is not effective if a subvalvular embolus is present.

4. A method of attack in the treatment of subvalvular type of pulmonary arterial obstruction is postulated.

5. When hypotension occurs during surgery along with failure of recovery from anesthesia, pulmonary embolism should be suspected.

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Simultaneous Pulmonary Resection for Bronchiectasis and Commissurotomy for Mitral Stenosis

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THE question of whether commissurotomy should be performed in a patient with lung disorder is often raised. The two cases presented herein indicate that such surgery is not only feasible but also practical. In over 1,000 cases of mitral commissurotomy only two have had sufficient bronchiectasis to merit surgery. This is surprising in view of the fact that the etiology of rheumatic fever is associated with a streptococcal infection of severe degree. Left-sided bronchiectasis and mitral stenosis may be operated upon concomitantly, provided the patient is in fairly good physical condition as in Case 1. This is diagrammatically illustrated in Figure 1.

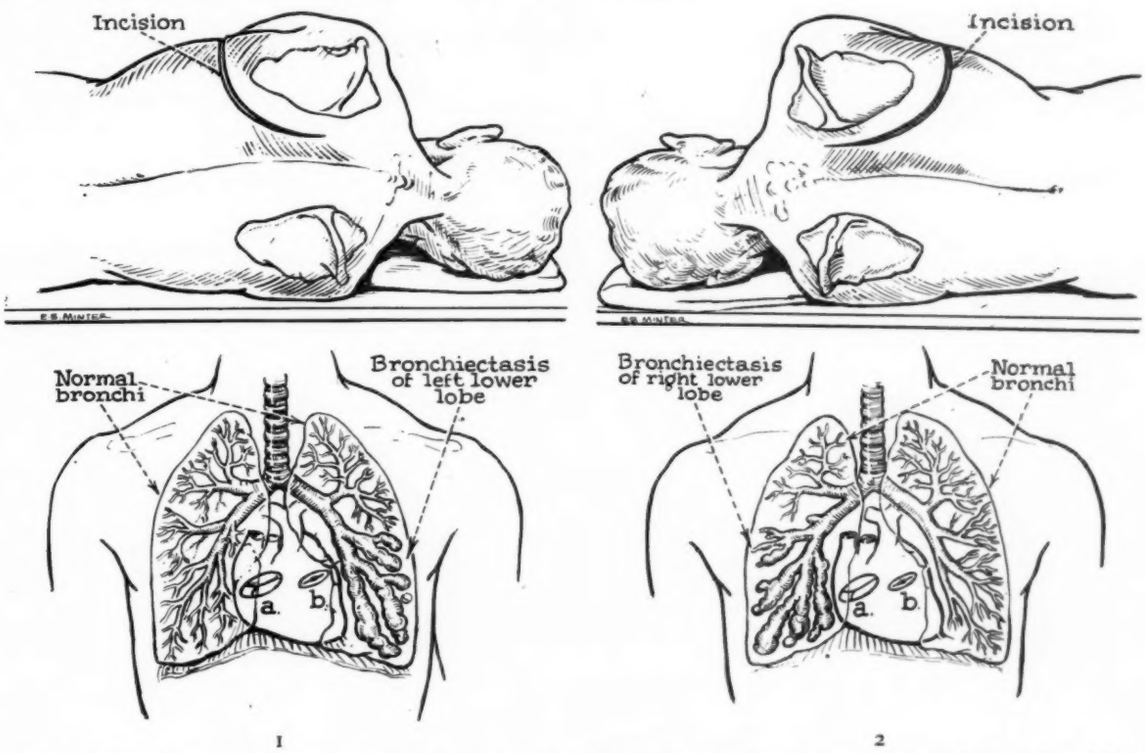


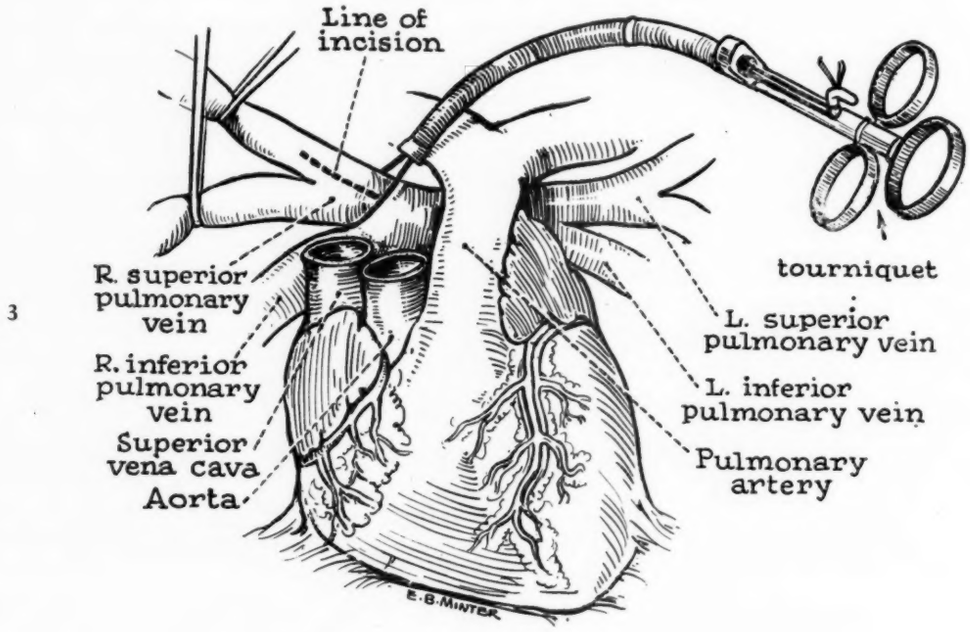
FIG. 1. Surgical exposure for mitral commissurotomy and left lobectomy is adequate in the left lateral position. (*a*) Normal tricuspid valve; (*b*) stenosed mitral valve.

FIG. 2. Surgical exposure for mitral commissurotomy and right lobectomy is adequate in the right lateral position if the mitral valve is approached through the right superior pulmonary vein. (*a*) Normal tricuspid valve; (*b*) stenosed mitral valve.

Mitral stenosis complicated with right-sided bronchiectasis could be approached through the right pulmonary vein as suggested by Neptune et al.[1] (Figs. 2–4.) However, in the

approach through the right superior pulmonary vein the palpable anatomy of the mitral valve is reversed from that of the left lateral position. The occasional operator as well as the experienced one can easily become confused.

For the occasional operator we believe it is better to stage the procedure. In the two-stage approach it is our opinion that mitral commissurotomy should be performed first for the following reasons: The left lateral position is almost a necessity for performing an adequate mitral commissurotomy. In performing mitral



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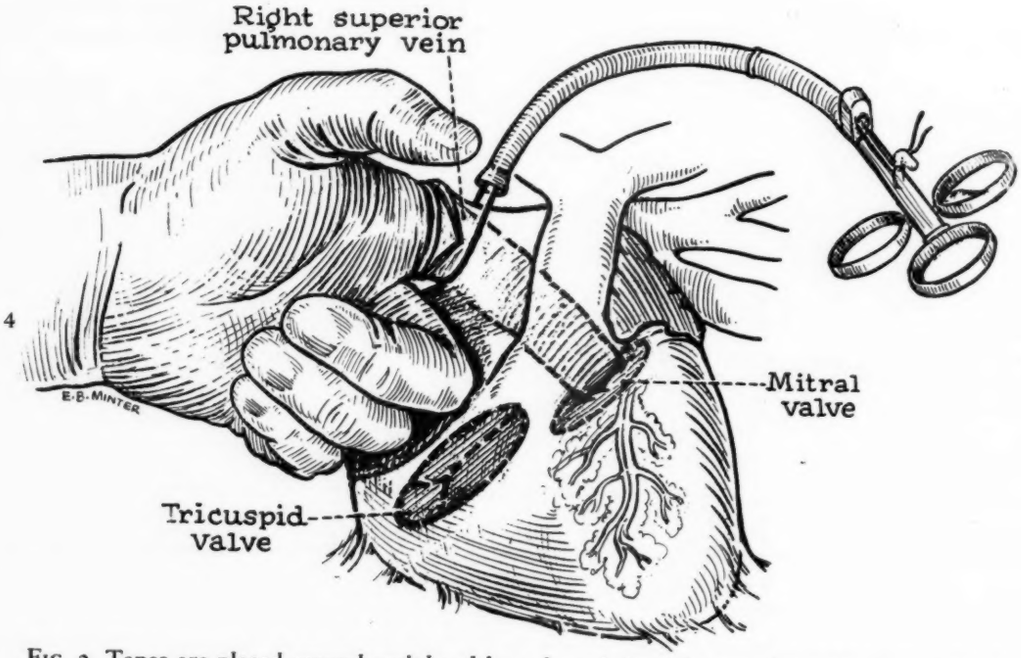

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FIG. 3. Tapes are placed around peripheral branches of the right superior pulmonary vein. A purse-string suture is placed in the adventitia of the right superior pulmonary vein and connected to a Romel tourniquet.

FIG. 4. Mitral commissurotomy using the digital technic.

commissurotomy it is necessary to collapse a large portion of the left lung. If a large portion of the right lung had been previously removed for bronchiectasis, it may not be possible to adequately oxygenate the patient.

Mitral stenosis complicated with bilateral bronchiectasis could be handled as in Case II.

Important aspects of postoperative care are: (1) The staff should be alert to the presence of retained secretions in the tracheobronchial tree. These can be handled by intratracheal aspirations or by bronchoscopy. (2) Restriction of fluids because of diminished lung tissue. (3) On signs of incipient failure one should digitalize and give thiomerin and aminophyllin simultaneously. This is well illustrated in Case II.

CASE REPORTS

CASE I. Mrs. D., a twenty-five year old white woman, was referred from the Thoracic Clinic for possible cardiothoracic surgery. She denied history of rheumatic fever. Her heart murmur had been detected when she was eight years old in the course of a routine examination at school. She had been short of breath for over ten years. For the past four years she had been getting pain from across the back of the chest. Any exertion would bring about chills and fever ranging from 102 to 104°F. which disappeared with rest. Her trouble started getting worse two years previously with progressive diminution in exercise tolerance. At the time of admission she could hardly do her housework or even walk two city blocks. She became orthopneic, with swelling of the ankles towards evening. She never had nocturnal dyspnea or attacks of pulmonary edema.

Physical examination revealed a tall, thin female of twenty-five in no acute distress. The chest was symmetric with equal expansion of both sides. Examination of the heart revealed sharp M-1, a mid-late diastolic murmur and accentuated P-2, with a normal sinus rhythm. Examination of the lungs revealed normal breath sounds on the right side with crackling rales over the left base.

Systemic review was essentially negative except for positive findings just described. Electrocardiogram tracings were within normal limits.

Ear, nose and throat, and bronchoscopy consultation revealed normal trachea and larynx; normal, thin, pulsating undisplaced carina, and normal right and left main bronchi. Much mucopurulent material was expelled and aspirated from the left lower bronchi. The branch lower lobe bronchi were somewhat dilated. Smears made from the secretion were fixed in alcohol-ether solution and sent to the laboratory for cell study. Bronchography was performed on the same day. The smears made from the bronchus showed numerous normal respiratory cells along with occasional larger pigment-laden macrophages and scattered polymorphonuclear leukocytes. No malignant cells were identified.

X-ray studies revealed a prominent pulmonary conus segment. Slight left atrial enlargement with encroachment on the barium-filled esophagus was detected on the right anterior oblique studies. Bronchogram revealed good visualization of the bronchial tree of both lower lobes and the right middle lobe. The right middle and lower lobe pattern appeared normal. However, there was marked cylindric bronchiectasis of the inferior portion of the left lower lobe. A few small sacculations were visualized at this site. The minor bronchioles were dilated along their length.

Laboratory data revealed the following: hemoglobin 87 per cent; total white blood count 7,400; hematocrit 46 cc.; sedimentation rate 29 min.; prothrombin time 20 seconds, 75 per cent of normal. Blood serology was negative for Wassermann and Kahn. Blood urea nitrogen 15 mg.; sugar 122 mg.; total protein 6 gm.; albumin 3.9 gm.; globulin 2.10 gm.

Urinalysis revealed a yellow, cloudy, alkaline specimen with specific gravity of 1.015. Albumin and sugar were negative. Microscopic examination revealed many epithelial cells and a few white blood cells per high power field.

Sputum studies were negative for acid-fast bacilli. A few gram-positive cocci and a few gram-negative bacilli were found.

The history, clinical, electrocardiographic, bronchoscopic and x-ray studies pointed to a diagnosis of rheumatic heart disease with mitral stenosis and bronchiectasis of the left lower lobe, while the laboratory data and preanesthetic consultation indicated that the patient was a good risk for mitral commissurotomy and left lower lobectomy.

Left lower lobectomy and mitral commissurotomy were performed. There was no thrombus of the auricular appendage or calci-

fication of the mitral valve. There were a considerable number of adhesions over the apex of the left upper lobe, in addition to dense fibrous bands over the diaphragmatic surface. The basal segments of the left lower lobe were nodular with trapping of air in them.

Histologic examination of the left lower lobe showed bronchiectasis with interstitial fibrosis, chronic passive congestion and pulmonary arteriosclerosis.

The patient's postoperative course was stormy. Her blood pressure was stable to 100/70 soon after her return from the operating room and she had a quiet first night. Her blood pressure the next morning was 100/80. Her apical rate was 93 to 96 per minute. X-rays showed a density in the right upper lung field which was reported by the radiologist as pneumonitis. She was expectorating blood-tinged sputum effectively. Scattered over her back were some sibilant and sonorous rales. The ventricular rate was 100 per minute. There were a few extrasystoles. The heart sounds were perfect and no murmurs could be detected. Her general condition was good. The next day, as she was fibrillating, our cardiologist prescribed quinidine, 6 gr. every four hours. By 10:00 P.M. she had normal sinus rhythm with a ventricular rate of 100 per minute. Her temperature was 102.2°F. By midnight the blood pressure fell to 86/0. Quinidine was stopped at once. By 12:45 A.M. the pressure was still 88/44. She seemed more comfortable by 4:00 A.M. She had a few coughing spells and her blood pressure was 92/40. She was coughing large amounts of mucopurulent material. By the fourth postoperative day the periods of hypotension alternating with periods of well-being were getting less frequent. Temperature had come down to 99°F. The next day her hemoglobin was 52 per cent, white blood count 17,850 per cu. mm. X-rays showed a density at the left base. Her temperature rose to 102°F. by evening. In view of these findings 500 cc. of whole blood were ordered and started at 10:00 P.M. On the sixth postoperative day her temperature was normal and she was able to cough better. However, by 10:30 P.M. of the same evening she was acutely dyspneic following the blood transfusion. She was noted to have been raising blood-stained sputum. Her pulse and apical rates were each 120 per minute. M-1 was sharp. There were bilateral basal rales. A tracheal suction was performed with aspiration of a large amount of mucus. Oxygen was given but there was no relief. Cedilanid, 0.4 mg., was given intramuscularly and 0.8 mg. was given intravenously. Aminophyllin, 7½ gr., was given by slow intravenous injection. Thiomerin, 2 cc., was given intramuscularly. A portable chest film revealed pulmonary arterial engorgement with enlargement of the cardiac silhouette suggestive of congestive failure. Following this therapy the patient was considerably improved. The next day at 6:00 A.M. her temperature was 99°F. and pulse 104 per minute. She slept well in the course of the night. She was put on a maintenance dose of digitoxin, 0.2 mg. daily. Her sutures were removed on the twelfth postoperative day. From this point on her postoperative course was uneventful. She was finally discharged on the twentieth postoperative day.

Follow-up notes one year and three months later reveal that the patient responded well to surgery. Following surgery she has had very little expectoration, only one to two teaspoonsful of mucoid sputum daily. On physical examination her lungs were clear, she had no complaint of cough and her exercise tolerance had improved considerably. She was not taking any drugs.

CASE II. B. P., an eighteen year old white girl, was admitted October 14, 1949, for possible cardiopulmonary surgery. History revealed that this patient had had a chronic cold since the age of two, and had had a persistent cough between the ages of two and six. Because of her persistent cough at the age of six she had been admitted to a sanatorium as a case of tuberculosis. Sputums were negative. She was discharged at the end of two years. Her cough and productive sputum persisted (300 cc. daily). She had blood-streaked sputum on several occasions. Her activities were restricted.

At fourteen years of age she had had pneumonia and was hospitalized for fourteen days. Following pneumonia the cough persisted, more during the evening, and continued to be more productive. She adhered to postural drainage for an indefinite length of time. Under medical supervision she was treated with penicillin tablets and inhalation therapy during the summer of 1949 before being finally referred for surgery.

Physical examination revealed a poorly nourished white girl in no acute distress.

Pertinent findings of the chest examination were as follows: Restricted expansion of the left hemithorax; diffuse rales over the left lower lobe; diffuse rales over the right middle lobe area; a few rales were also present over the right lower lobe area, but of a lesser degree. The cardiologist noted a diastolic thrill over the apex, a sharp M-1, a presystolic accentuation of a mid-late diastolic murmur, and also noted that for some unknown reason the P-2 was not accentuated.

Preoperative bronchograms revealed: (1) Saccular bronchiectasis of the right middle lobe and the inferior division of the right lower lobe; (2) Saccular bronchiectasis of the inferior division of the left lower lobe and the lingula.

Electrocardiogram findings were within normal limits.

Cardiac catheterization studies were as follows:

	Maximum (mm. Hg)	Minimum (mm. Hg)
L.P.A.	31.9/25.8	27.7/17.8
R.V.	27.7/6.4	25.2/5.1
R.A.	4.5/.6	

Left lower lobectomy, lingulectomy and mitral commissurotomy were performed on November 2, 1949. Lobectomy with lingulectomy was performed first and the bronchial stump was covered over with the mediastinal pleura. The upper lobe could be expanded well. As the patient was in good condition, it was decided to enlarge her mitral opening at once. The mitral valve was found to be soft and flexible; it could barely admit the tip of the index finger. The right heart knife was introduced to the region of the mitral valve opening and two cuts were made on the anterolateral commissure. The mitral valve could very easily admit the index finger, and no attempt to enlarge the valve at the posterior commissure was made. The patient withstood the operative procedure well and was returned to her room in good condition.

The chest tube was removed at the end of forty-eight hours. The left lung was well expanded. X-rays taken on November 5, 1949, showed a slight pneumothorax and two fluid levels. Thoracentesis yielded 350 cc. of serosanguineous fluid. Pericardial friction rub was heard from November 12th until November 21st. Some mucopurulent material was obtained from the left upper lobe. Following the procedure the mobility of the chest wall improved as did the patient's condition. She was discharged on December 3, 1949.

This patient was readmitted on August 7, 1950. Physical examination revealed no dyspnea. In the lungs numerous moist rales over the right lower lobe and right middle lobe areas were heard. No wheezes were heard, nor were there signs of fluid or pleuritic rub. The heart revealed a systolic murmur, grade 1, P-2 greater than A-2. There was a history of frequent upper respiratory infection (ten to twelve episodes). If the patient hurried or increased her activity she tired easily, which she did not preoperatively.

Resection of the basal division of the right lower lobe and right middle lobe was performed on August 10, 1950.

Two days later at 3:30 A.M. the patient was dyspneic. Many mucous rales in the right and left side of the chest were heard. Breath sounds decreased on the right side. Bronchoscopy was performed. A large quantity of mucopurulent secretion was aspirated from the left upper lobe bronchus. The mucous membrane was inflamed, especially on the left side. The right bronchus main stem was partially obstructed by a large plug of mucous which was aspirated. The wheezing was controlled by an injection of 250 cc. of 5 per cent glucose in water with 7½ gr. of aminophyllin. The next day she was able to cough and raise secretions well. By August 14th the wheezing had decreased and her breathing had much improved.

Thoracentesis on August 18th, yielded 150 cc. of serosanguineous fluid. The patient was noted to have more dyspnea on August 20th. Fluoroscopy revealed fluid at the right base. Thoracentesis yielded 200 cc. of serosanguineous fluid. The next day this dyspnea was more marked. The liver was tender, but palpable. Scattered rales were present over both lung fields. The patient had tachycardia and raised 1½ ounces of sputum in twenty-four hours. Bronchoscopy was performed on August 22nd. Secretions from the left upper lobe bronchus were aspirated. The next day thoracentesis yielded 100 cc. of blood-tinged fluid.

Bronchoscopies had to be performed on September 11th, 13th, 15th, 18th and 20th. The amount of secretion progressively dimin-

ished and she was discharged on September 21, 1950.

She was readmitted on March 8, 1951, for bilateral bronchogram and postoperative check-up.

She had frequent colds all winter. Sputum was reduced by 50 per cent, and was never foul. Dyspnea showed no change. She gained only 2 pounds. Her appetite remained the same. There were many rales and wheezes over the posterior lower chest (superior division right lower lobe).

Examination of the heart revealed grade I–II mitral systolic murmur, no diastolic. She was improved slightly subjectively.

Bronchograms on March 9th revealed the anterior bronchus of the right upper lobe to be dilated and cylindric. No bronchiectasis was visualized on the left. Bronchographic findings were consistent with a good result.

Follow-up notes on October 27, 1952, revealed that the patient stated she had had some residual cough which was productive of a minimal amount of mucoid sputum. The quantity had diminished considerably since her surgical procedure. She felt somewhat stronger, although she said that she was prone to catch cold. The patient had moderate dyspnea on ascending twelve steps, but could walk three to four blocks without appreciable dyspnea.

Physical examination revealed blood pressure of 145/70. Auscultation of the heart showed a normal sinus rhythm, a very sharp first sound at the mitral area. Examination of the lungs revealed fine moist rales at the left lower lateral lung field which cleared with cough. The chest was otherwise clear.

On fluoroscopic examination the patient had a surprising aeration of her lung, considering the extensive amount of surgery which had been performed. The right diaphragm moved rather sluggishly but the left was normal; and there was no abnormal density in either lung field. The pulmonary artery was quite prominent. The heart appeared of normal size.

On June 7, 1954, follow-up notes stated that the surgery had been very successful. The patient was still performing posture drainage morning and night. However, after her posture drainage she expectorated only 2 to 3 teaspoonfuls of mucoid sputum. She was taking no medication. She was working as a secretary and had to walk to the bus and then several blocks to the office. She was moderately short of breath on climbing a flight of stairs but was perfectly able to carry on her work. She had no cough or hemoptysis and no more than an occasional cold.

SUMMARY

1. A plan of surgical treatment of concomitant bronchiectasis and mitral stenosis is presented.

2. The low incidence of concomitant bronchiectasis with mitral stenosis is mentioned.

3. Attention is called to the importance of postoperative bronchoscopy, adequate digitalization and restriction of fluids in the postoperative management.

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*Swartout, R., III, and Gunther, K.: "Dizziness:" Vertigo and Syncope, GP *8*:35 (Nov.) 1953.

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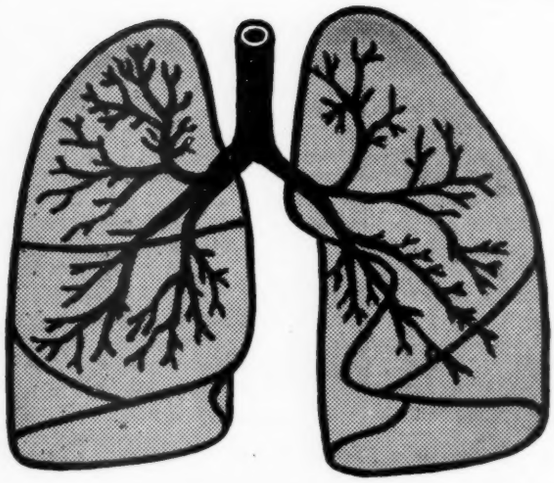

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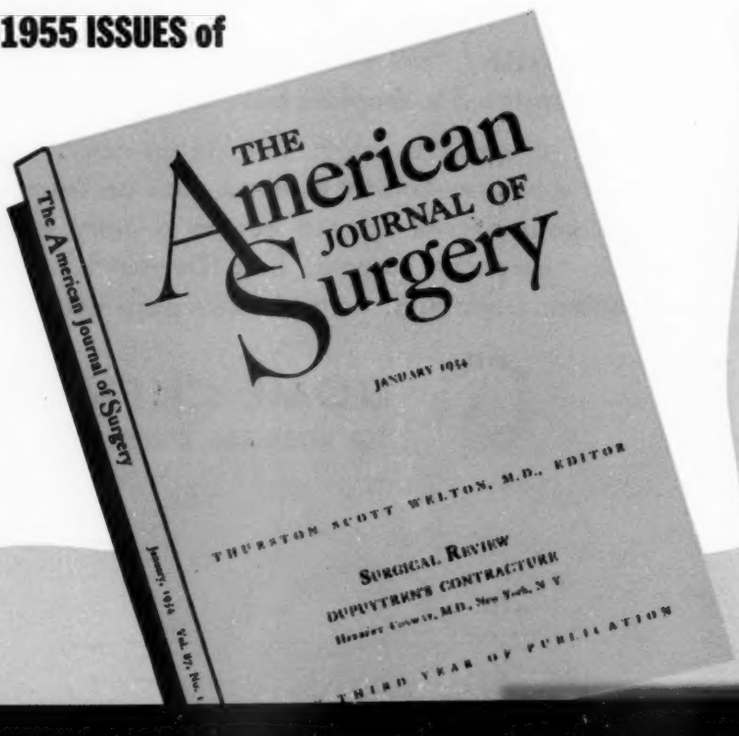

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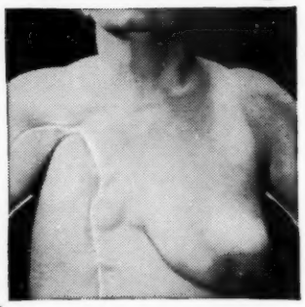

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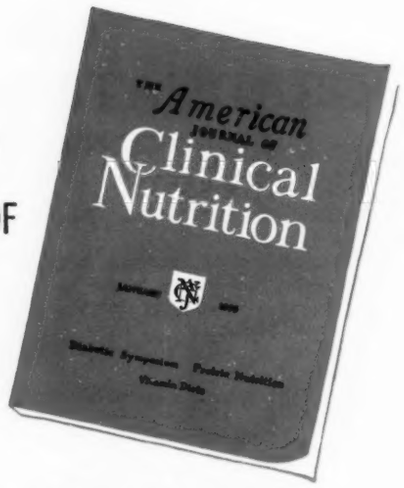

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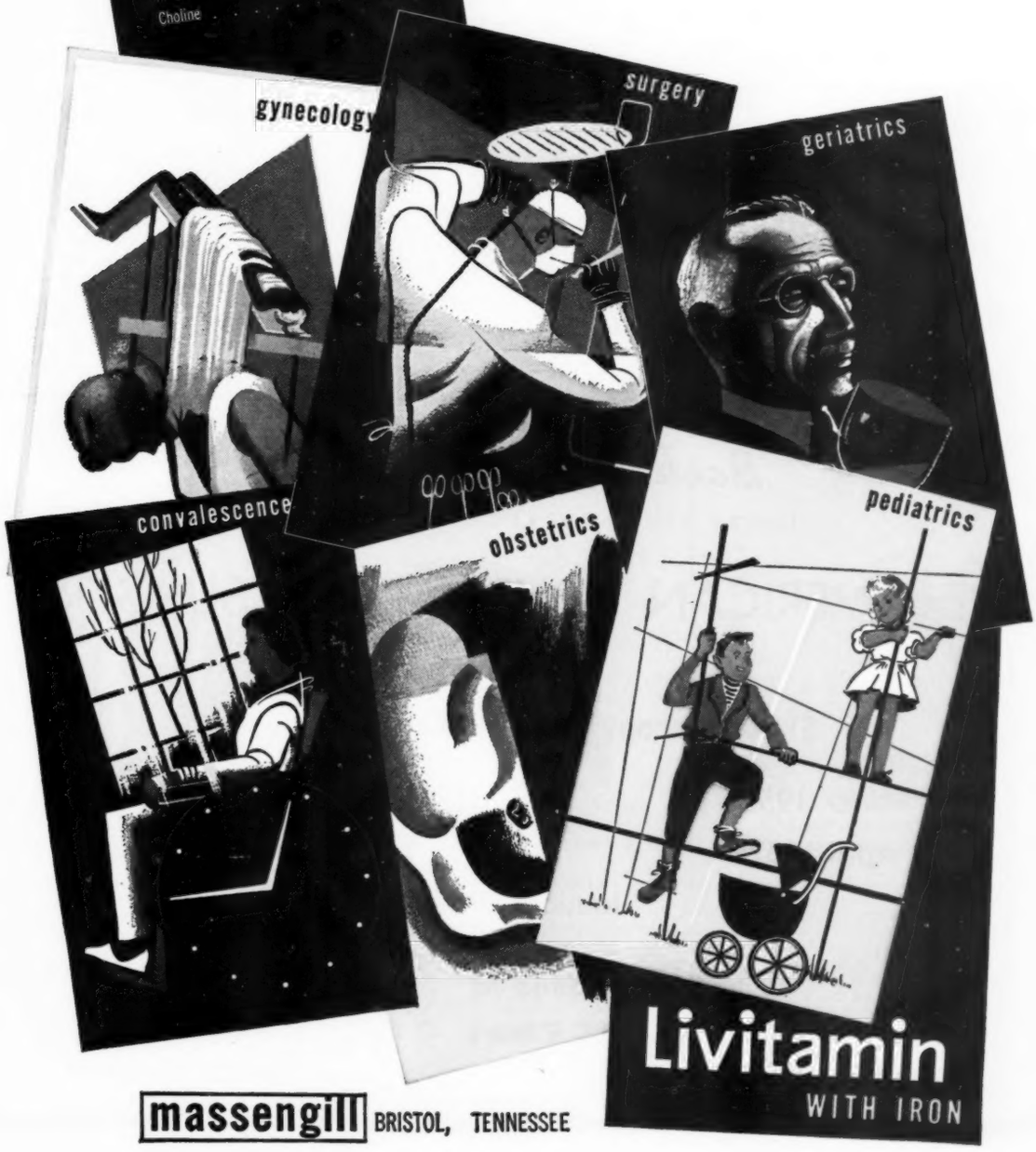

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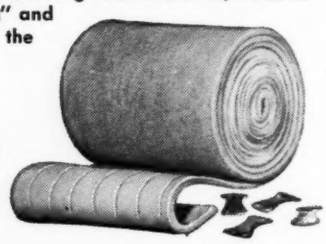

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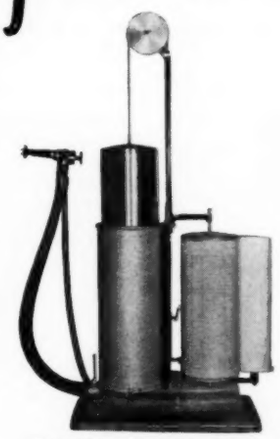

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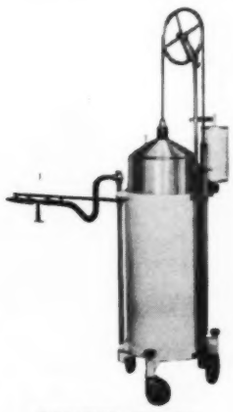

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NOTES AND QUOTES

The American public is often demanding maximum health services "without willingness to accept the necessary responsibilities or obligations" in the opinion of Dr. Willard C. Rappleye, Dean of Columbia University's Faculty of Medicine in his annual report to the President of the University.

Dr. Rappleye devotes considerable attention to "The National Health Problem" and particularly to the question of "adequacy" of health services. He states further that "'adequacy' cannot be a fixed idea because it will vary from time to time and from situation to situation. It cannot be a purely theoretical consideration because as one goal is reached new targets are developed."

In explanation the Dean emphasizes the importance of retaining "the good and strong features of proven methods of practice." But, he notes, to these must be added "social, economic, political and administrative devices that will extend and make available to the entire population the latest methods of diagnosis, treatment and prevention."

These ends, the Dean says, can be accomplished "only in competition with other demands upon the disposable income of families and through various methods for voluntary savings, with particular reference to persons of moderate means who today are so largely living on installment buying."

Dr. Rappleye further states that "one of the major considerations in the evolution of the concept of health services is the transition from the established methods of individual, solo private practice of medicine on a fee-for-service basis into a modernized plan consistent with the recent developments in specialization within the profession, the requirements for extensive resources for the modern practice of medicine and the necessity of distributing the high costs of health services through various prepayment and insurance plans."

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A REPORT on the first thirty years of the "Yale Plan of Medical Education," a method of study which differs in many respects from that of most American medical schools, appeared in the September issue of *The Journal of Medical Education*. Dr. Vernon W. Lippard, Dean of the Yale University School of Medicine and President-Elect of the Association of American Medical Colleges, is the author of the report which indicates the plan has been extremely successful in developing initiative and independent thinking among Yale medical students.

In the mid-twenties the Yale medical faculty introduced a program in which the medical student was treated as a graduate student and given more than customary responsibility for his own development. The goals of this plan were "to strengthen the qualities of integrity, intelligence, capacity for work, common sense and a faculty of ascertaining the truth."

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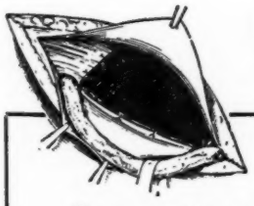

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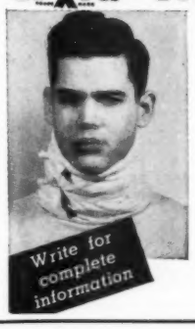

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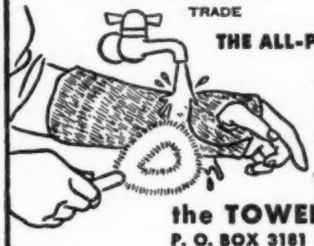

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Dr. Lippard believes that the Yale plan has been a success, since the students have established and maintained an excellent record in the national board examinations, successful completion of which is the threshold requirement at Yale for advancing from the preclinical to the clinical years, and for graduation. Yale's record compares favorably with the other medical schools.

According to an announcement from the American Medical Writers' Association, the first four-year collegiate courses in medical journalism and writing leading to a bachelor's degree will be inaugurated next September at the University of Illinois, Urbana, and the University of Missouri, Columbia. Several partial scholarships ($500 each), sponsored by the American Medical Writers' Association, will be available. Dr. Harold Swanberg, Quincy, Ill., Secretary of the Association, has initiated the fund with a $1,000 contribution to establish one scholarship at each of the schools. Checks for the fund should be made payable to the Association and marked for the Medical Journalism Scholarship Fund. Descriptive literature concerning the academic courses may be obtained from Earl F. English, Ph.D., Dean, School of Journalism, University of Missouri, Columbia, and I. W. Cole, School of Journalism and Communications, University of Illinois, Urbana. (J. A. M. A., 155: 499, May 29, 1954.)

PHOTOGRAPHIC "3-D maps" that show doctors the labyrinthine interior of the human head and neck have been published by a Stanford University professor of anatomy and his photographer-collaborator. Consisting of 350 color-film transparencies, the publication climaxes five years of work by Dr. David L. Bassett of Stanford and William B. Gruber of the publishing firm of Sawyer's, Inc., Portland, Oregon.

With startling clarity the color films show organs, nerves, muscles, blood vessels and connective tissues in their natural spatial relation to each other. When given a "3-D" quality by the "View Master," a modern stereoscope invented by Gruber, the anatomic views take on a graphic vividness not seen even in a medical dissecting laboratory. One reason for this realism is the meticulous preparation of progressive dissections by Dr. Bassett. Special embalming methods are employed to preserve tissue colors. Arteries are filled with red latex rubber for easy identification, veins with blue. Other reasons are the quality of modern photographic materials, as well as Gruber's specially developed photo technics and his stereoscopic viewer. The transparencies can also be projected on a screen for a larger audience to see in "3-D" through polaroid glasses.

Each photograph in the series is duplicated in an artist's pen-and-ink drawing on which all parts are labelled. This enables the doctor to identify unmistakably the most minute details. More than 700 pages of drawings, descriptive text and an index of over 8,500 references are contained in five volumes that accompany the transparencies.

The new photographs comprise the second published section of Dr. Bassett's "Stereoscopic Atlas of Human Anatomy." The first section, showing the central nervous system in 238 three-dimensional views, was released two years ago. Dr. Bassett said five more sections will be published to complete the atlas. He estimates this will take another four to five years.

Medical authorities have received the atlas with widespread praise. It has proved an invaluable teaching aid at Stanford School of Medicine and elsewhere and is providing an unequalled anatomy reference work for physicians, surgeons and medical scientists generally.

The National Foundation for Infantile Paralysis announces the availability of a limited number of postdoctoral fellowships in medicine and the related biologic sciences. These fellowships are awarded as a part of the National Foundation's

CONTINUED ON PAGE 48

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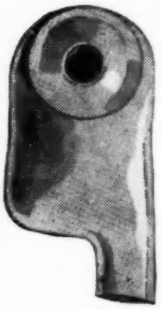

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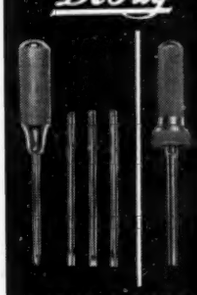

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Eligibility requirements include: an M.D., Ph.D., or equivalent degree, U.S. citizenship (or application for citizenship) and sound health. Selection of candidates will be made on a competitive basis by the National Foundation's Fellowship Committee. Fellowships will be awarded for a period of one to three years and in rare instances may be extended to five years. Stipends ranging from $3,600 to $7,000 a year are allowed, the specific sum being determined by marital status and number of dependents. The institution in which the Fellow receives his training may request compensation of $500 to $1,000 a year.

For consideration by the Fellowship Committee in February, applications must be received by December 1st; for consideration in May, applications must be filed by March 1st; for consideration in November, by September 1st. For further information and application blanks address: The National Foundation for Infantile Paralysis, Division of Professional Education, 120 Broadway, New York 5, N. Y.

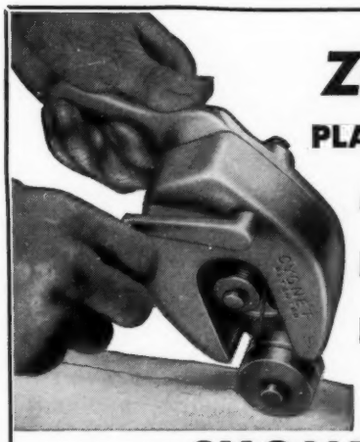
A "SECOND LOOK" at the well known "blue baby" operation which has brought relief to many hundreds of children born with defective hearts was a feature of the Second World Congress of Cardiology. Dr. Helen B. Taussig of Johns Hopkins Hospital, Baltimore, who with Dr. Alfred Blalock originated this surgical procedure in 1945, led a discussion of a five-to-eight year follow-up of the first 500 operations performed at this hospital. The discussion followed presentation of a detailed statistical analysis by Drs. Benjamin D. White, Daniel G. McNamara and Richard Bauersfeld, which indicated that two-thirds of those improved by the operation maintained their gains several years later. It has been emphasized in the past that although the operation brings dramatic improvement in many cases, it is not a complete cure.

One of the heart defects from which "blue babies" may suffer is an abnormal narrowing of the outflow tract through which "used" or deoxygenated blood leaves the right side of the heart on its way to the lungs for fresh oxygen. The skin of these children takes on a bluish tinge because the oxygen content of the blood supplying the tissues is too low. The procedure devised by Drs. Blalock and Taussig produces a shunt or by-pass of the narrowed area by joining one of the arteries arising from the aorta, the main artery of the body, to a branch of the pulmonary artery which carries deoxygenated blood to the lungs. With the volume blood flowing into the lungs greatly increased, the body's oxygen supply improves and "blueness" diminishes or disappears.

The report presented by Dr. White and his associates offered complete information on the present state of 255 of the first 500 patients subjected to this procedure at Johns Hopkins Hospital. Two hundred forty-four had obtained original improvement from their operation, classified as "good" in 226 cases and "fair" in eighteen, according to Dr. White. Five to eight years later the number who had maintained a good result was 163, or just about two-thirds. Fourteen dropped down into the "fair" group; nine are "no longer improved"; twenty-three required and survived a second operation; thirty-three died. (The last group are additional to the eighty-one of the original 500 who died at or within six months of operation.) The patients who maintained a good result showed normal exercise tolerance, said Dr. White, and a more or less stable circulatory condition.

A more recent alternative to the Blalock-Taussig operation—which is performed outside the heart—involves a direct attempt to get more blood to the lungs by removing, rather than by-passing the obstruction. In this procedure, developed by Sir Russell Brock of England, the heart itself is entered and the constricted tissues widened by cutting. Drs. Don M. Hosier and John L. Pitts of Baltimore, joined by Dr. Taussig, analyzed the post-operative results of this procedure in sixty-nine

CONTINUED ON PAGE 50



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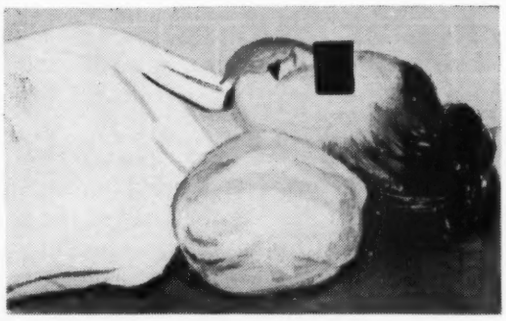

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patients who have been followed for periods varying between three months and four years. Virtually all, they said, showed "a striking increase in exercise tolerance." Other changes suggested that the strain on the right side of the heart (which must work extra hard to force the blood through the narrowed areas) had been significantly reduced for a majority.

The physicians termed the operative risk of the Brock procedure "remarkably low" (there were seven deaths during or shortly after surgery, of a total of eighty-six operations performed). Their conclusion: "All patients who survived operation have shown some definite evidence of improvement."

New examinations have been announced by the U. S. Civil Service Commission for filling Medical Officer positions in certain Federal agencies as follows: Positions of Medical Officer, paying $5,940 *and* $7,040 *a year and Medical Officer (Specialist), paying* $8,360 *to* $10,800 *a year, will be filled in various agencies in Washington, D. C. and vicinity, and in the U. S. Public Health Service and the Children's Bureau, located throughout the United States. Positions of Medical Officer paying* $7,425 *to* $10,450 *a year will be filled in the Panama Canal Company-Canal Zone Government Organization in the Panama Canal Zone.*

To qualify for these positions, applicants must be graduates of a medical school with the degree of Doctor of Medicine. For most of the Medical Officer positions at the entrance level, applicants must have completed a full internship. For Medical Officer (Specialist) positions, applicants must have completed appropriate study or residency training in the specialized field of medicine for which application is made. Professional medical experience is required for the higher-paying positions. No written test is required.

Full information regarding these positions is given in Announcement No. 415 for Medical Officer, Announcement No. 414(B) for Medical Officer in the Panama Canal Zone, and Examining Circular EC-27 for Medical Officer (Specialist). These notices may be consulted at most post offices or copies may be secured direct from the U. S. Civil Service Commission, Washington 25, D. C. Applications for all positions will be accepted until further notice. Applications for all positions will be accepted until further notice. Applications for positions in agencies in the United States must be filed with the Commission's Washington office. For positions in the Panama Canal Zone, send applications to the Board of U. S. Civil Service Examiners, Balboa Heights, Canal Zone.

CONTINUOUS presentation of rectal or esophageal temperature during and after surgery, particularly important in cases involving induced hypothermia, is made conveniently possible by a Thermistor, or highly temperature-sensitive electronic semi-conductor, incorporated in a new device called a Tele-Thermometer.

The Thermistor, manufactured by Carboloy Department of General Electric Company, Detroit, transmits it minute electrical variations to a large dial on the instrument which indicates temperature directly. The device is equipped with a ten-foot flexible probe lead, so that insertion may be made at any point without the inconveniences associated with an ordinary glass thermometer on the operating table.

In addition to low-temperature surgery, the device finds application in operations involving children, neurosurgery and long or critical procedures. It is also a versatile clinical and diagnostic instrument for peripheral vascular disease and therapy, skin temperature determination in physical therapy, monitoring the effects of nerve blocks, sympathectomies, vasoconstrictors and vasodilators, and post-operative temperature monitoring.

Developed and manufactured by the Yellow Springs Instrument Co., Inc., Yellow Springs, Ohio the Tele-Thermometer is a very simple instrument without vacuum tubes or delicate galvanometers, and draws its power from a single standard flashlight cell. The instrument has a temperature range from 68 to 108°F., accurate to 0.4°F.

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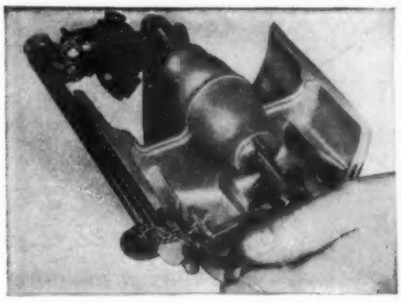

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1. Allen, E. V.; Barker, N. W.; Hines, E. A., Jr.; Kvale, W. F.; Shick, R. M.; Gifford, R. W., Jr., and Estes, J. E., Jr.: Medical Treatment of Essential Hypertension, Proc. Staff Meet., Mayo Clin. *29*:459 (Aug. 25) 1954.
2. Livesay, W. R.; Moyer, J. H., and Miller, S. I.: Treatment of Hypertension with Rauwolfia Serpentina Alone and Combined with Other Drugs, J.A.M.A. *155*:1027 (July 17) 1954.

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